SOME REACTIONS OF

ACETYLENIC ALCOHOLS

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by

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ABSTRACT

PART I

Reactions of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7) with lithium aluminium hydride in a range of ethers as solvent gave only two products: 1-methoxy-2,2-dimethyl-3-phenylhexa-3,4-diene (C4) and (E)-1-methoxy-2,2-dimethyl-3-phenylhex-4-en-3-ol (C3). The relative yields of the products varied with solvent as well as with reaction conditions. However, deuterium labelling revealed that the ratio of hydride attack at the C4 and C5 of the alkyne function remained constant. Reactions of compound (B7) in benzene as solvent were found to give reasonable yields of the two products (C3) and (C4).

Reactions of 1-methoxy-3-phenylhex-4-yn-3-ol (B4) with lithium aluminium hydride in diethyl ether gave 1-methoxy-3-phenylhexa-4,5-diene (C5), and (E)-1-methoxy-3-phenylhex-4-en-3-ol (C6) as the predominant product. In the tetrahydrofuran reactions at room temperature only compound (C6) was identified. Under more vigorous conditions, the alkynol (B4) was converted into two cyclopropane derivatives (C7) and (C8) in addition to the major product (C6). The mechanisms for the formation of these cyclopropane derivatives are discussed.

PART II

Reactions of 4-t-butylcyclohexanone and its methylated analogues (2.2, 2.7, 2.9, 2.10) with propynyl-

magnesium bromide or propynyllithium gave the alkynols (B8, B9, B10, B11, B12, B13, B14, B15). The stereochemistry of these reactions ~~are~~ is discussed.

The reductions of the above alkynols with lithium aluminium hydride in a range of ethers as solvent were investigated. Compounds (B8-13) reacted to give the corresponding allene, (Z)-alkenol and (E)-alkenol; (D1-18). The reactions of compound (B14) gave allene (D19) and (E)-alkenol (D21), no cis alkenol was detected. Allene (D19) was produced predominantly. Alkynol (B15) reacted to give the two usual products (D22, D24) but, in addition gave the secondary alcohol (B16). The mechanism of formation of compound (B16) is discussed. The reactions of alkynols (B13, B14, B15) in diethyl ether as solvent gave the corresponding allenic compound (D16, D19, D22) as the sole product.

GENERAL INTRODUCTION

Only over the last few years have the lithium aluminium hydride reduction of some propargyl alcohols been examined closely in order to obtain stereochemical and mechanistic information. In the reduction of propargyl alcohols with lithium aluminium hydride, two major reaction pathways are often followed. The first reaction pathway leads to the formation of an allenic compound. The early synthesis of allenes dates back to 1888 and involved dehydrohalogenation of a 1,2,3-tribromo derivative, followed by removal of the bromine from the dibromo olefin with zinc[1a]. Fifty two years later a slightly better method was developed by Ginzburg[1b] who reduced 3-chloro-3-methyl-1-butyne (A1)* with a zinc-copper couple to obtain dimethylallene in a 63% yield. However, both methods are long and tedious, or suffer many drawbacks in the experimental procedures. An easy method to obtain allenes was soon demonstrated by Wotiz[1c] in the lithium aluminium hydride reduction of 3-bromo-1-heptyne (A2). Since then many allenic compounds have been synthesized in good yield, employing lithium aluminium hydride in the reduction of propargyl alcohols of which some have the common structural features as summarized in (1) (Scheme 1).

Probably the first propargyl alcohol of this type which was found to give an allene was discovered by Bailey and Pfeifer[1d] in 1955 when they reacted 4-chloro-2-butyn-1-ol (A3) with lithium aluminium hydride. One year

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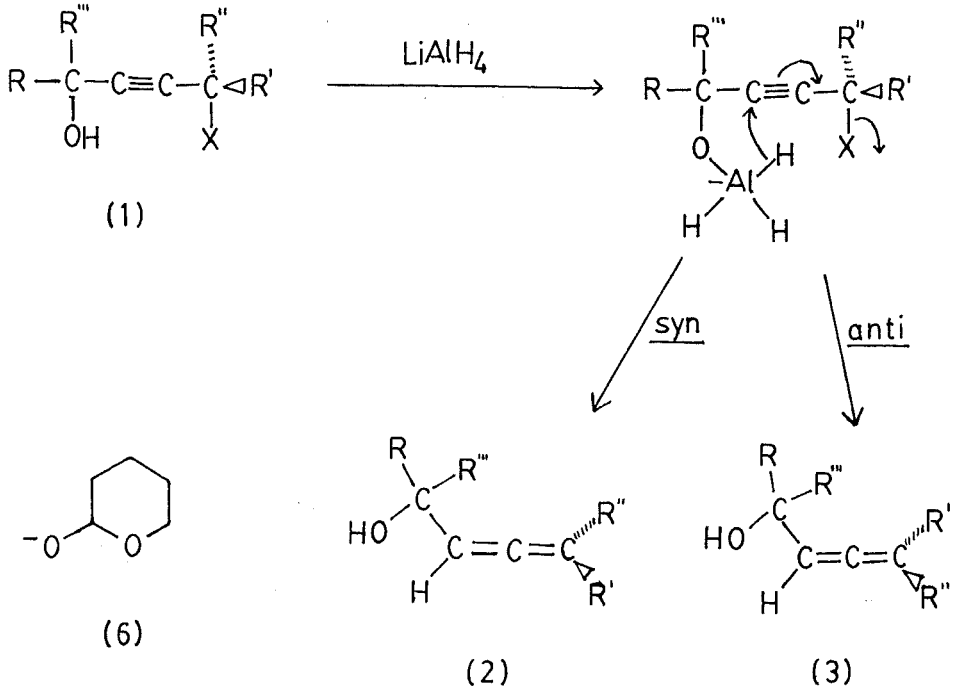
* Figure given in Block A.



(1) (6) (2) (3)

Scheme 1

later Miki[1e] reported that the reduction of 1,4-dihydro-oxyacetylene (A4) with lithium aluminium hydride also yielded an allene.

Two conceivable mechanistic pathways are plausible for the above type of reaction which yields allenes. The first is the synchronous S_Ni' mechanism which is outlined in Scheme 1. The initial hydride attack on the hydroxy group results in the formation of the oxygen-aluminium bond with evolution of hydrogen. The function of the aluminium bound to the oxygen is to donate a hydride ion intramolecularly to the near carbon* of the alkyne function with a concerted shift of an electron pair and the departure of the group X. The group X may be a hydroxyl group which leaves as $^-OAlH_2$[1e,2], a tetrahydropyranyloxy group which leaves as (6)[3,4,5], a tertiary alkylammonium group which

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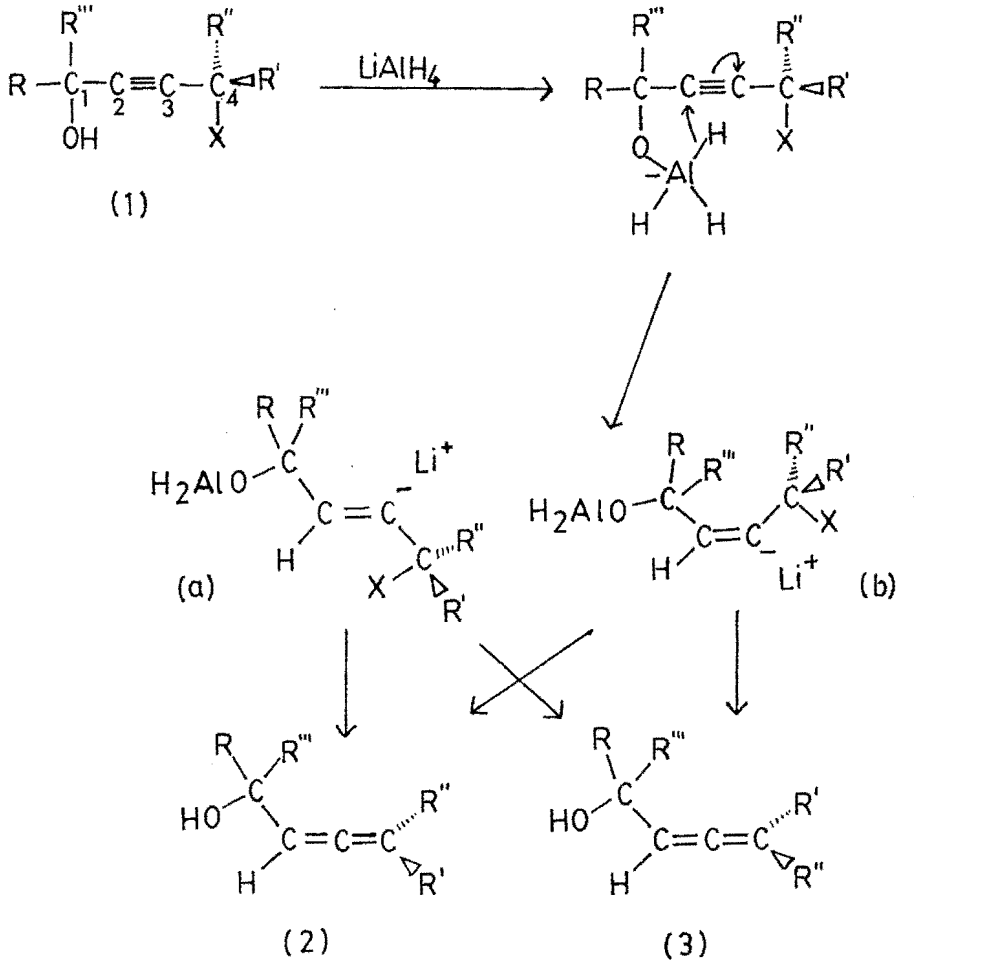
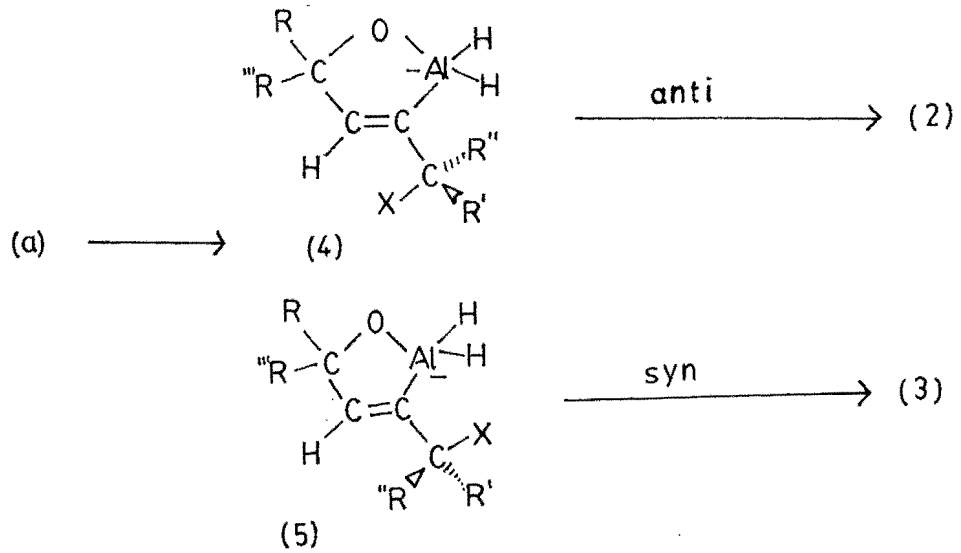
* It refers to the carbon of the alkyne function nearest to the alkoxyaluminium hydride group.

leaves as $PhCH(CH_3)NMe_2$[5], an alkoxy group which leaves as $^-OR(R=n\text{-}C_3H_7,\ t\text{-}C_4H_9$ or $(C_2H_5)_2N\text{-}(CH_2)_2)$[4], a chlorine group which leaves as Cl^- [6,1(d)] or an oxiran oxygen atom which leaves as an alkoxide[7]. The stereochemistry of the departure of the group X could occur either cis or trans to the incoming hydride ion, which leads to the diastereomeric allenes (2) and (3) respectively.

The second alternative mechanism S_N2', which is analogous to the S_N2' reactions in the allylic systems, involves an addition elimination process. The reaction mechanism is given in Scheme 2. The first step of the reaction is the same as in Scheme 1 which involves the formation of the oxygen-aluminium bond with evolution of hydrogen. The alkoxyaluminium hydride function then donates a hydride ion to the near carbon of the alkyne triple bond leading to two stable carbanions (a) and (b) which may be stabilized by counterions in the reaction medium. Subsequent attack by the electron pair on C4 followed by elimination of the group X gives the diastereomeric allenes (2) or (3). A vinylic organoaluminium intermediate (4) or (5) could be formed from carbanion (a). Allene (2) is formed by anti elimination of (4) and syn elimination of (5) gives allene (3). However, evidence for the existence of carbanions (a) and (b) and for this mechanism has yet to be presented.

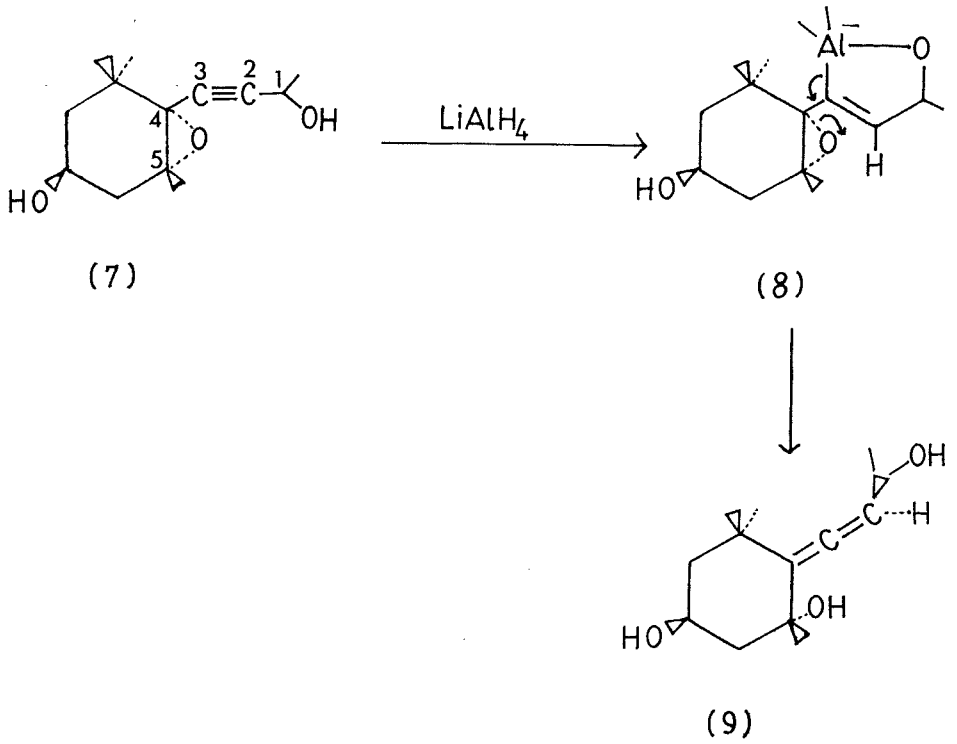
Both the syn and the anti stereochemistry of the allene-forming 1,3-substitution reactions of the above chiral propargyl alcohols have been observed in their reductions with lithium aluminium hydride. Hlubucek et al[7] observed a syn substitution mechanism in the ring





Scheme 2

opening of a 4,5-epoxy-2-alkyn-1-ol derivative (7) with lithium aluminium hydride which afforded the α-allenic alcohol (9), see Scheme 3. In the reduction, the

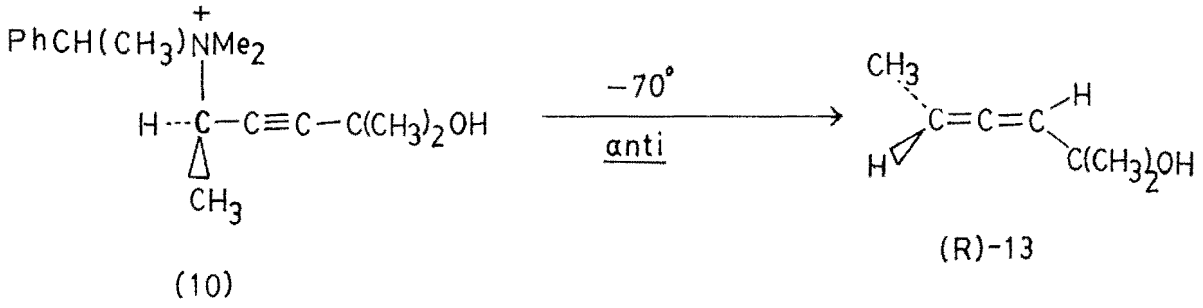


(7) (8) (9)

Scheme 3

intermediacy of an organoaluminium compound (8) was postulated to give the allene (9) having the tertiary hydroxy group at C5 trans to both the other hydroxy groups. Thus the reaction of lithium aluminium hydride with the alkyne results in insertion of a hydrogen atom at the position α- to the propargylic hydroxyl group, and cis to the departing propargylic oxygen substituent. Recently Claesson and Olsson[8] noted that reduction of the chiral propargylic trialkylammonio derivative (10) with lithum aluminium hydride in tetrahydrofuran at -70° yields the α-allenic tertiary alcohol 2-methyl-3,

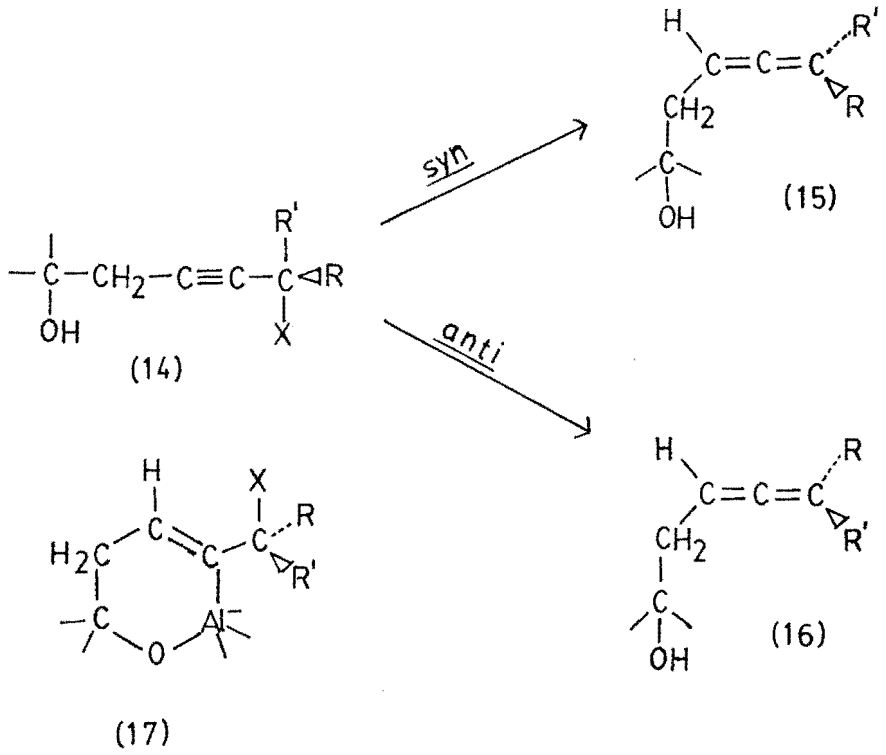
4-hexadien-2-ol (13, Scheme 4) in a preferred anti stereochemical course.



(10) (R)-13

Scheme 4

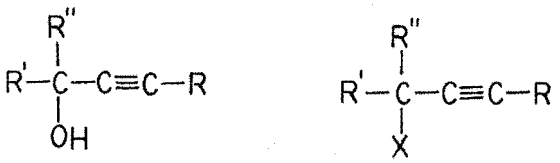
Another type of propargyl alcohols with common structural features as summarized in Figure (14) has been synthesized recently[5,9]. The group X may be an alkoxy group, a tetrahydropyranyloxy group or a



Scheme 5

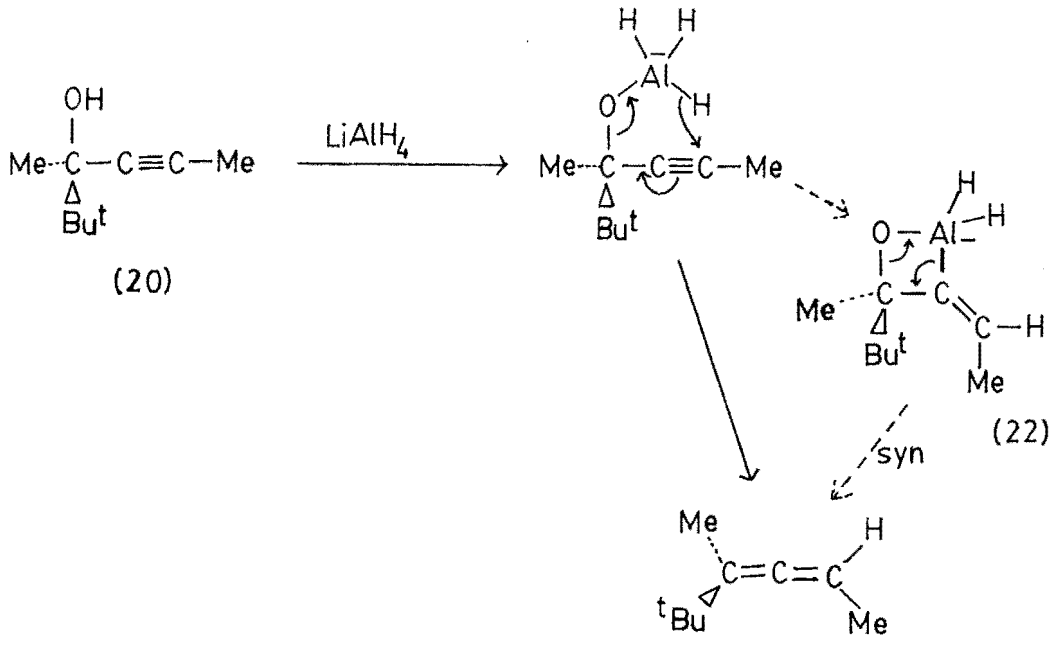
quaternary amine group. β-Allenic alcohols are prepared by the reaction of these propargyl alcohols with lithium aluminium hydride. For these reductions two reaction mechanisms are possible, the S_Ni' mechanism or a stepwise S_N2' type of reaction involving the six-membered ring intermediate (17). So far the lithium aluminium hydride reductions of only two chiral derivatives of this type of system have been reported, which could lead to an understanding of its stereochemistry of displacement. In both cases β-allenic alcohols were formed via a <u>syn</u> mechanism[5].

Allenes can also be formed by hydride reduction of a slightly different structural acetylenic alcohol as summarized in (19). One example which can be used to illustrate the stereochemistry of the allene-forming mechanism is the reaction of (R)-(+)-2,2,3-trimethyl-hex-4-yn-3-ol (20) with lithium aluminium hydride in refluxing diglyme[10]. The relative stereochemistry of the optically active alkynol (20) and the chiral product, 4,5,5-trimethylhexa-2,3-diene (21), are consistent with a synchronous S_Ni' reaction mechanism. The initial step of the reaction is the same as in Scheme 1 which involves the coordination of the aluminium atom to the hydroxyl oxygen with the immediate liberation of hydrogen. The single hydroxyl group which has been modified to $-O\overset{\ominus}{A}lH_3$, first donates



(19)

(23)



(20)

(22)

(21)

(S)-(−)-allene

Scheme 6

a hydride ion to the far* carbon of the alkyne function and simultaneously leaves as $OAlH_2^{\ominus}$ in the formation of the (S)-(-)-allene (21). The concertedness of the S_Ni' reaction requires that the hydride attack at C5 must necessarily occur <u>syn</u> coplanar to the hydroxyl group. However, it is not possible to exclude an alternative stepwise S_N2' mechanism in which the labile organoaluminium

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* It refers to a carbon of the alkyne function furthest away from the alkoxyaluminium hydride function.

intermediate (22) was formed and by syn elimination could lead to the same stereochemical result. Other propargyl alcohols of this type of structure, 1,1-diphenylbut-2-yn-1-ol (A5)[17] and 2-phenylpent-3-yn-2-ol (A6)[18] have been shown to give allenes on reaction with lithium aluminium hydride in other solvents such as diethyl or di-isopropyl ether.

Propargylic compounds lacking a hydroxyl group can also give allenes upon reaction with lithium aluminium hydride or aluminium hydride (AlH_3). The structural system is given in (23) (Scheme 6), where X can be a chloride group[1d], a bromide group[1c,8], or a dialkyl-ammonium group[8]. The reaction seems to follow a concerted S_Ni' mechanism in the formation of allene. Thus, the overall stereochemistry is predominantly a syn displacement of the leaving group X. The reaction mechanism is similar to that given in Scheme 6 in which the initial stage involves the association of the leaving group with the hydride reagent to give an ion pair and subsequently hydride attack on the triple bond results in the concerted expulsion of group X.

The stereochemistry of the allene-forming pathway of the various structural propargylic systems mentioned above may be dependent on several factors:

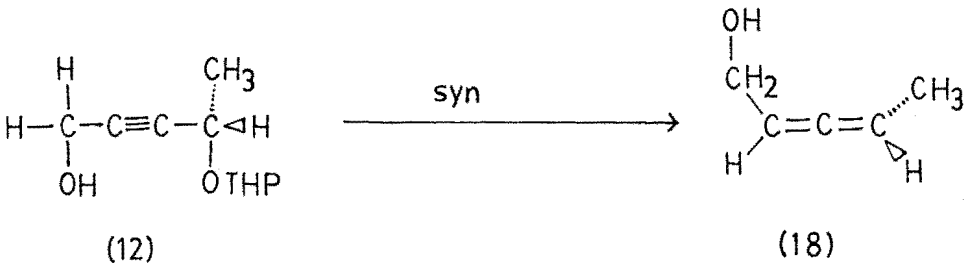
a) The nature of the hydride reagent used. Thus, Borden and Corey[11] observed a syn substitution in the allene-forming reduction of chiral 1,3-di-tert-butylpropargyl alcohol with lithium aluminium hydride/aluminium chloride (mole ratio 3:1), whereas with $LiAlH_4$-$AlCl_3$ (mole ratio 13:1) it underwent an anti displacement mechanism. A tendency towards an anti mode of substitution was also noted in the

reaction of (S)-dec-3-yn-2-ol with an increasing mole ratio of $LiAlH_4$-$AlCl_3$[8], i.e. a decrease in the amount of $AlCl_3$.

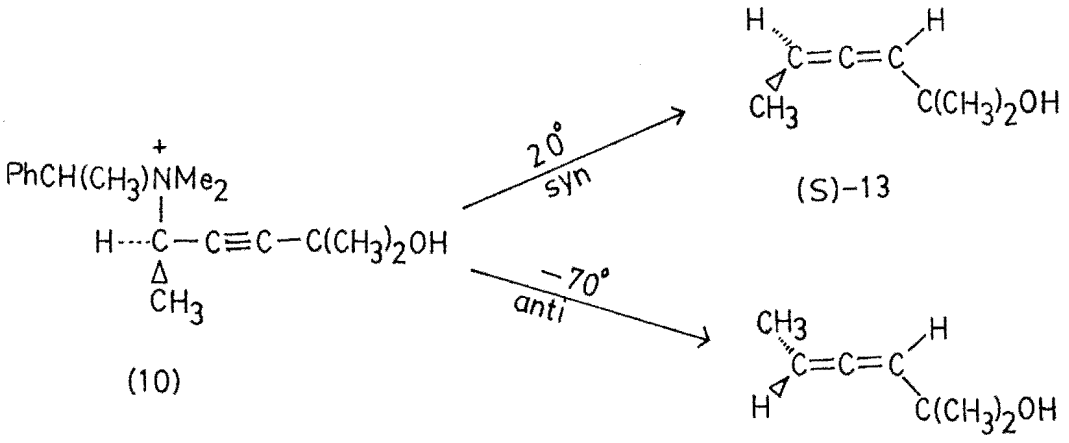
b) The solvent employed. The formation of the α-allenic alcohol (18) by lithium aluminium hydride reduction of compound (12) proceeded by an overall syn substitution (Scheme 7). It was shown that increasing donor properties of the solvent, from di-isopropyl ether through diethyl ether to tetrahydrofuran, increased the overall stereoselectivity of the reaction[5].

c) The temperature of the reaction.[8] At 20° in tetrahydrofuran as solvent the chiral propargylic tri-alkylammonio derivative (10) reacted with lithium aluminium hydride in a predominant syn displacement to give the α-allenic alcohol (S)-13, see Scheme 7. At lower temperature (-70°) a very high anti-syn ratio of 85:15 was observed. However, the enantiomeric yields were unaffected in both the cases of the conversion of (24) → (25), see Scheme 7, at 0° and 35° in diethyl ether, and that of (26) → (27) at 20° and -70° in tetrahydrofuran. It is therefore concluded that the effect of reaction temperature on the sterochemical course is likely to depend on the nature of the leaving group as well as the position of the hydroxyl group.

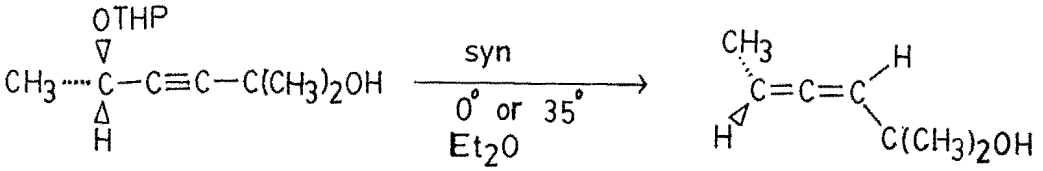
The second reaction pathway in the lithium aluminium hydride reduction of propargyl alcohols is common to most substrates and involves the formation of allylic alcohols which may have the cis or trans stereochemistry. The reaction mechanism is outlined in Scheme 8. The initial step of the mechanism involves the conversion of the



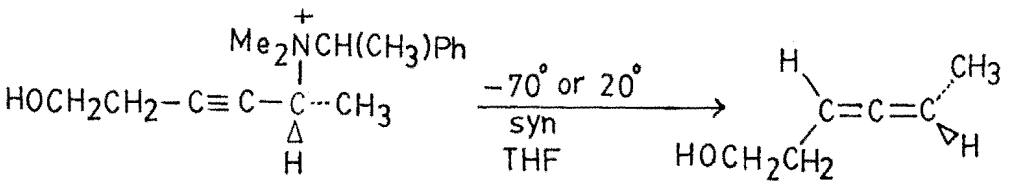
(12) (18)



(10) (S)-13 (R)-13

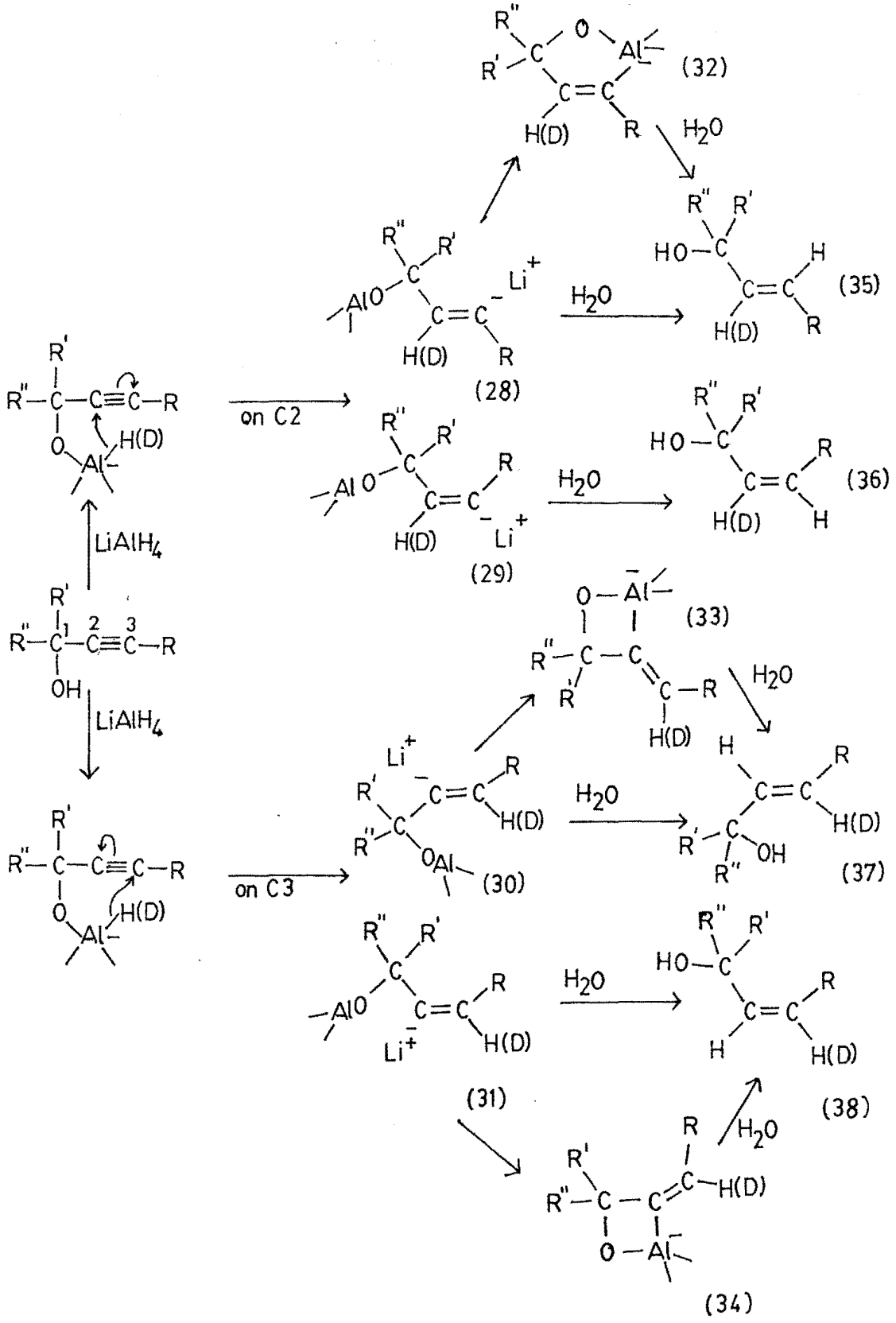


(S)-24 (R)-25



(R)-26 (S)-27

Scheme 7



Scheme 8

hydroxy group into an alkoxyaluminium hydride which may donate a hydride ion intramolecularly to either carbon of the acetylenic linkage. This intramolecular hydride transfer is supported by the experimental fact that 1-t-butyl-3-phenyl-propargyl alcohol was 38% reduced whether 3 or 6 moles of lithium aluminium hydride were used[12]. Hydride transfer to C2 or C3 will result in the formation of 4 stereochemically stable vinyl carbanions (28), (29), (30), (31), which have the cis or trans configuration, being stabilized by any available counterions (depicted here as Li^+) in the reaction medium. Upon the addition of water these carbanions give cis or trans alkenols (35), (36), (37), (38). However, carbanions (28), (30) and (31) may gain extra stabilization in the formation of the 5-membered or 4-membered cyclic organoaluminium species (32), (33) and (34) respectively prior to hydrolysis.

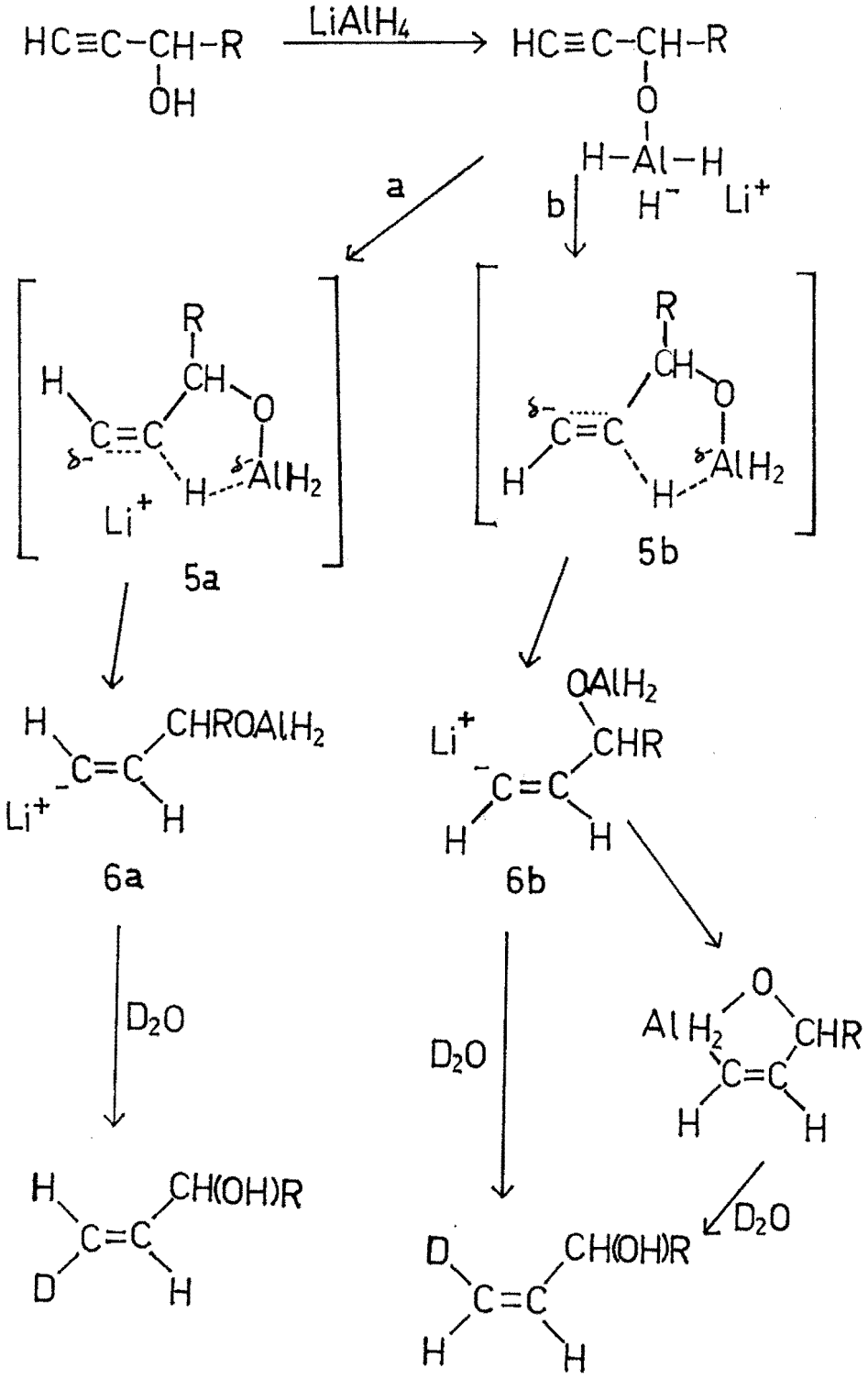
Borden ~~et al~~ [12] first noted that the cis/trans product ratio of the allylic alcohols obtained upon lithium aluminium hydride ($LiAlH_4$) reduction of 4,4-dimethyl-1-phenylpent-1-yn-3-ol (A7, block A) was markedly solvent-dependent. In tetrahydrofuran as solvent an exclusive product was formed which was identified as the trans alkenol (A8) while the use of diethyl ether as solvent led to the formation of some 25% cis alkenol (A9) in addition to the expected trans alkenol.

Grant and Djerassi[14] explored more extensively the effect of solvent on the stereochemistry of reduction of 1-heptyn-3-ol (A10, block A). Their results were rather surprising in that they showed a reciprocal relationship between solvent basicity and the

extent of cis reduction. With dioxane or tetrahydrofuran as solvent the corresponding trans alkenol was formed exclusively, but with diethyl ether or n-propyl ether cis reduction occurred to about 50% and for di-isopropyl ether cis reduction predominated over trans reduction to the extent of a 3:1 ratio. Their results are summarized in a table below.

SOLVENT	% trans reduction	% cis reduction
Dioxane	100	0
Tetrahydrofuran	100	0
2,5-Dimethyltetrahydrofuran	55	45
2,2,5,5-Tetramethyltetrahydrofuran	33	67
Ethyl ether	60	40
n-Propyl ether	50	50
Isopropyl ether	25	75

Since there was such a strong inverse correlation between the extent of the cis reduction and the ability of the solvent to solvate Lewis acids in the reaction medium, it was argued that the stabilization of the vinyl carbanions must have been influenced by the Lewis acids, see Scheme 9. They postulated two transition states (5a) and (5b) which lead to trans and cis vinyl carbanions (6a) and (6b) respectively. In the presence of stronger Lewis bases (e.g. dioxan, tetrahydrofuran) the Li^+ counterions are expected to be highly solvated and thus unavailable for the stabilization of developing anionic centers. Pathway (b)


HC≡C-CH-R
OH
LiAlH4
HC≡C-CH-R
O
H-Al-H
H⁻ Li⁺
a
b
R
CH
O
H
C≡C
δ-
H
δ-AlH2
Li⁺
5a
5b
CHROAlH2
H
C=C
Li⁺
H
6a
OAlH2
Li⁺
CHR
C=C
H
H
6b
D2O
D2O
AlH2
O
CHR
C=C
H
H
D2O
CH(OH)R
H
C=C
D
H
CH(OH)R
D
C=C
H
H

SCHEME 9

is therefore favoured since it involves the energetically more favourable transition state (5b) because of its greater separation of anionic sites. In weaker Lewis base solvents (e.g. ether, n-propyl ether) the Li^+ counterions are less solvated and hence readily available to stabilize the transition state (5a) which leads to cis alkenol. It is assumed that transition state (5a) will be more favourable than (5b) if Li^+ counterions are poorly solvated as in isopropyl ether.

The proposal is reasonable considering the fact that vinyl carbanions exhibit a high degree of stereochemical stability[15,16], which has been attributed to either sufficiently long life-times of the anion in its trigonal configuration or to the formation of stereochemically distinct intimate ion pairs with available counterions[16]. It was further substantiated by the experiment in which a small amount of crown ether, dicyclohexyl-18-crown-6, was added to isopropyl ether solvent in the reduction of 1-heptyn-3-ol. The result of this experiment showed a reverse in the cis:trans reduction ratio, (25:75) instead of (75:25). Pathway (b) is now favoured since the complexing of the lithium counterion by the crown ether[19] does not provide the necessary stabilization of the developing anionic centres in the transition state. Conversely, by lowering the temperature of the reaction to -25^{o} and extending the reaction time in diethyl ether the cis reduction increased by approximately 15% through pathway (a).

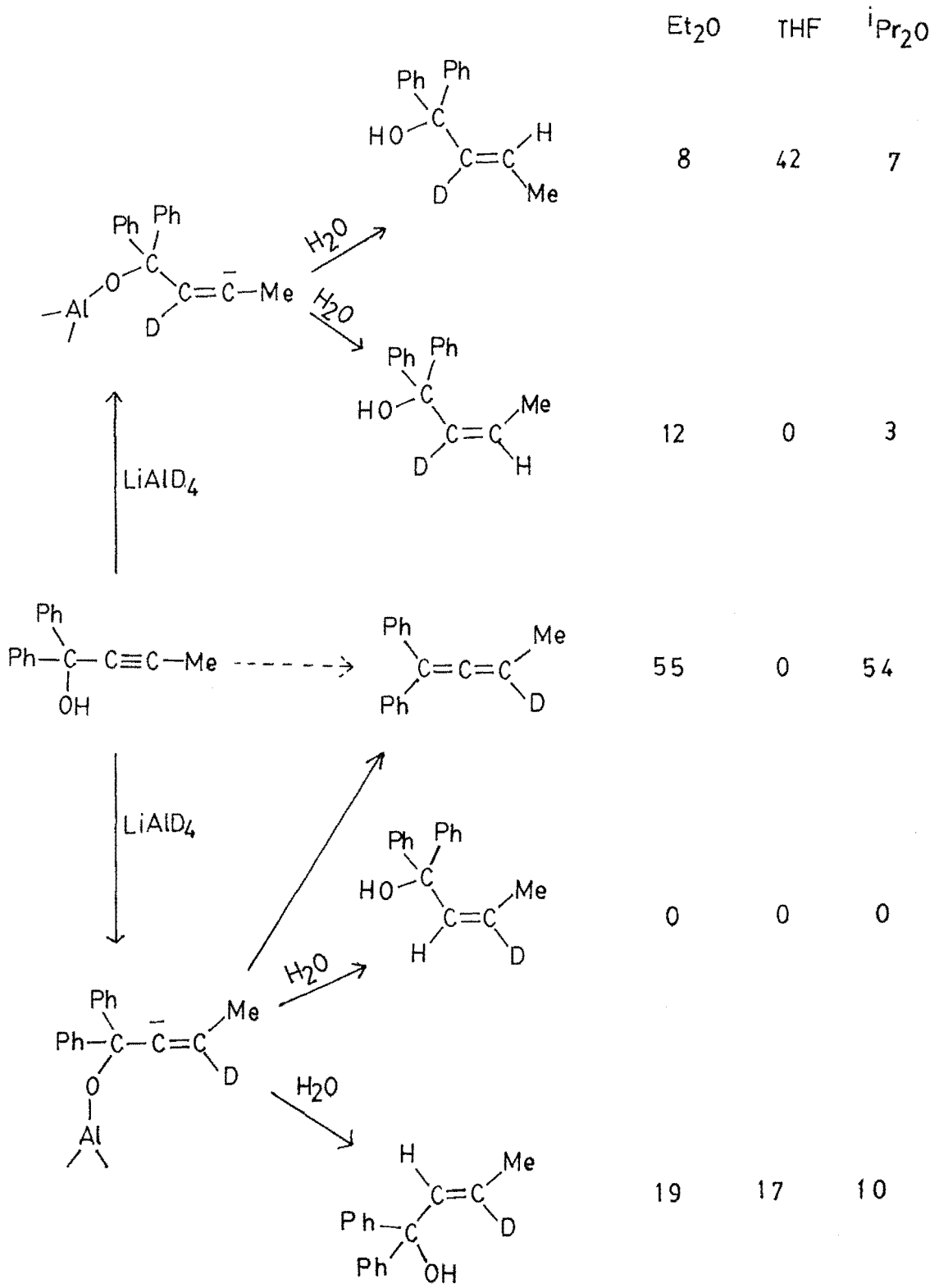
More recently, the above hypothesis was further examined employing mixtures of diethyl ether (Et_2O) and

tetrahydrofuran (THF) as the solvent for the reduction of 1,1-diphenylbut-2-yn-1-ol[17] (A5, block A). The ratios of products obtained were dependent on the solvent composition (see Table below). In addition to the formation of the (Z)-Alkenol (A11, block A) and (E)-Alkenol (A12, block A),

SOLVENT		Allene (B1) % yield	(Z)-Alkenol (A11) % yield	(E)-Alkenol (A12) % yield
Et_2O		55	12	27
Et_2O/THF	9:1	39	6	36
	3:1	15	2	48
	1:1	-	-	66
THF		-	-	59

the allene (B1, block B) was also isolated by chromatography. Nevertheless, cis reduction seems to increase gradually as the solvent mixture becomes richer in diethyl ether. Reaction in tetrahydrofuran as well as in a 1:1-mixture of diethyl ether and tetrahydrofuran yielded only a trans-alkenol (A12).

While in the past the reaction of propargyl alcohols with lithium aluminium hydride, without the addition of another reagent, always take place specifically with hydride added to the near carbon of the acetylenic group, in the above study the hydride transfer leading to alkenols is not site-specific, nor does the ratio of hydride attack at the two alkyne-carbons remain constant when the solvent is varied (Scheme 10). In another recent paper[20], the reduction of 2,2-dimethyl-3-phenylhex-4-yn-3-ol (B5, Block B) in diethyl ether gave only the corresponding allene which must result from far carbon attack, whereas in tetrahydrofuran, hydride attack


Et2O
THF
iPr2O
8
42
7
12
0
3
55
0
54
0
0
0
19
17
10
H2O
H2O
H2O
H2O
LiAlD4
LiAlD4

Scheme 10

occurs to twice the extent at the near alkyne-carbon atom, the results are tabulated below. As the temperature was increased from 35° to 65° in the tetrahydrofuran reactions,

TABLE Product yields of reactions of alkynol (B5) with lithium aluminium deuteride.

Solvant	Yield (%)		Attack by D' at near: far carbon	
temp.(°C), time(h)	Allene (C_1)	(E)-Alkenol (C2)	Leading to (C2)	Overall
Et_2O,35,89	84	Trace	-	ca.0:84
THF,35,89	30	60	60:0	60:30
THF,65,2.5	66	18	18:0	18:66
2,5-Me_2THF,65,2.5	92	2	2:0	2:92

the ratio of near:far hydride attack shows a reverse trend, with preference for far-alkyne-carbon attack at elevated temperature. A further significant increase in the near:far ratio was observed when 2,5-dimethyl-tetrahydrofuran was used, a solvent in which the ether oxygen atom is sterically more hindered. In all the reactions (E)-alkenol (C2) was formed by hydride attack specifically at the near alkyne-carbon atom.

The theory that the solvent is acting as a scavenger of counterions in the reaction medium is incapable of explaining the above results. It was therefore felt that there may be a specific role of the solvent taking a vital part in the mechanism of the reduction of propargyl alcohols with lithium aluminium hydride. For this reason Part I of this thesis is devoted to the task of exploring the

the nature of this other possible specific function of the solvent. Part II will deal with the effects of increased substitution at carbons 2 and 6 on the reactions of 4-tertbutyl-1-(prop-1′-ynyl)cyclohexanols.

PART I SOLVENT EFFECTS AND REACTIONS OF METHOXYALKYNOLS.

(a) Introduction.

It has been shown earlier that the relative amounts of carbanions (a) and (b) formed, refer to Scheme 11, are influenced by the solvent used, and it must be realized that the partitioning of the two reaction pathways leading to carbanions (a) and (b) occurs at the initial stage of the reaction. The complexing of the Li^+ counterions by the solvent therefore does not affect the directing of the hydride to the alkyne function, at least not initially. The only conceivable role of the ether solvent affecting the near:far carbon attack* must be the coordination of the solvent to the aluminium atom. In support of this view there was indication that tetrahydrofuran is able to coordinate to the aluminium atom in the preparation of aluminium hydride (AlH_3)[21] according to the equation given below. Aluminium hydride exists as a polymer in diethyl

$$(AlH_3)_n + nTHF \rightarrow nAlH_3 \cdot THF \qquad (1)$$

ether[45] but upon the addition of tetrahydrofuran (THF), a stronger Lewis base, the monomeric species is stabilised in solution as in Equation (1). Evidence indicative of the coordination of an internal ether to an aluminium atom had been reported by Eliel and Brett[22] in the isolation of two chelates (B2) and (B3), Block B. In the report, treatment of a mixture of cis and trans-4-methoxycyclohexanol

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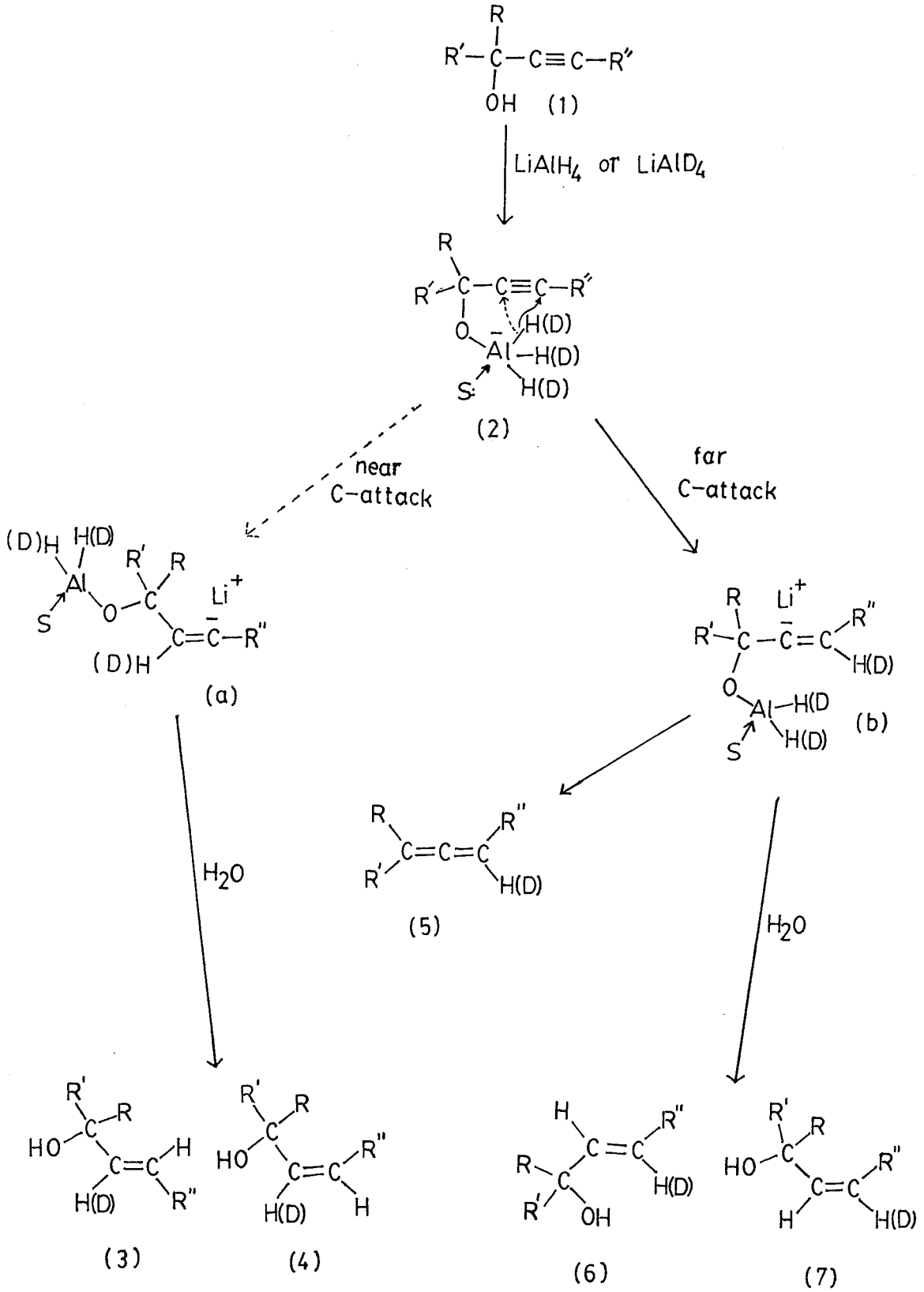
* Hydride attack on the near or far alkyne-carbons.


LiAlH4 or LiAlD4
near C-attack
far C-attack
H2O
H2O
(1)
(2)
(a)
(b)
(3)
(4)
(5)
(6)
(7)

Scheme 11

with the mixed hydride prepared from $LiAlH_4$ with $AlCl_3$ (1:4 mole ratio) gave only the cis chelate (B2). Similar treatment of cis- and trans-3-methoxycyclohexanol gave only the cis chelate (B3).

If the role of the ether solvent is such as described above then there arises the question of the coordination state of the aluminium atom in the reacting alkynyloxyaluminium hydride (2, Scheme 11). In the knowledge that aluminium prefers six-fold co-ordination to five-fold with highly electronegative atoms, it would mean that in this reduction process, two ether solvent molecules would be involved. In the subsequent discussion of Part I it can be shown that, in fact, there is direct evidence of at least one solvent molecule being attached to the aluminium atom making it at least five-fold co-ordinated prior to hydride transfer.

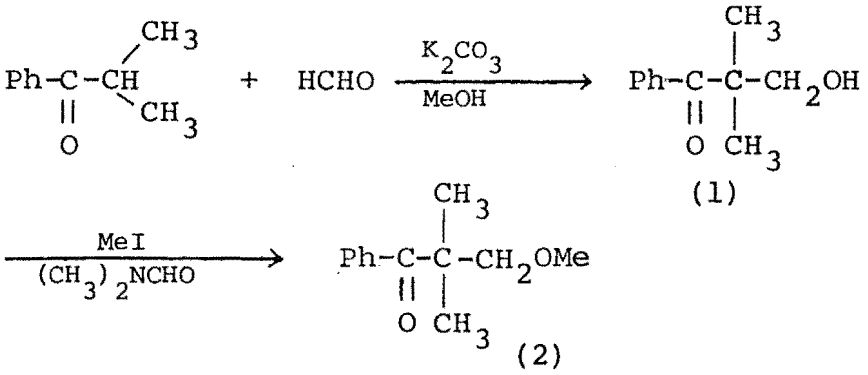
In order to examine the above-mentioned hypothesis two acetylenic alcohols with an internal ether were synthesized, 1-methoxy-3-phenylhex-4-yn-3-ol (B4), and 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7), Block B, and their reactions were studied with lithium aluminium hydride (or lithium aluminium deuteride) in a range of ethers as solvent.

(b) Discussion.

1-Methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7)

Alkynol (B7) which is an analog of 2,2-dimethyl-3-phenylhex-4-yn-3-ol (B5) with an internal ether, was synthesized in order to examine the solvent effect in the reduction of propargyl alcohols with lithium aluminium hydride. As was pointed out earlier, during the reduction of propargyl alcohol it was the solvent that was responsible for the ratio of hydride attack at the two alkyne-carbons due to its ability to solvate the aluminium atom of the alkynyloxyaluminium hydride. If this hypothesis holds true, this solvent effect would be nullified in the reduction of alkynol (B7) since the solvent molecule would be replaced by the methoxy group which is now acting as an internal ether that coordinates to the aluminium atom intramolecularly.

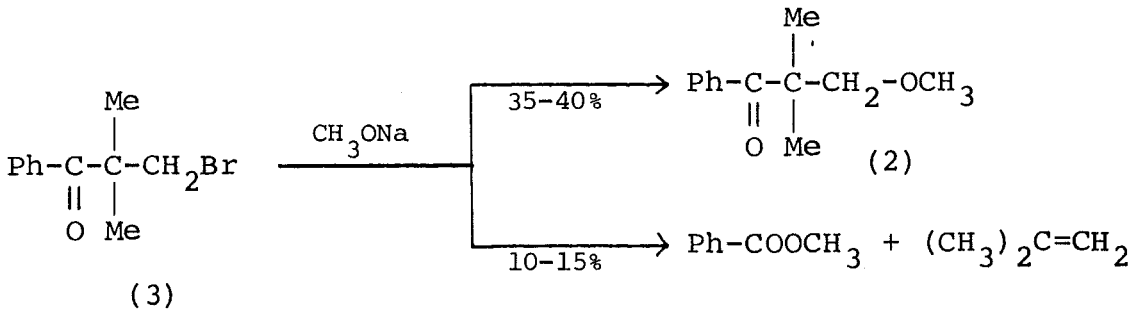
The synthesis of alkynol (B7) required the precursor, 1-methoxy-2,2-dimethyl-3-phenylpropan-3-one (2), and the preparation of propynyllithium. The synthetic route to methoxyketone (2) is outlined below. Aldol condensation



Scheme 12

of isobutyrophenone with formaldehyde was carried out under mild alkaline conditions to avoid side reactions such as the Cannizzaro reaction. The hydroxyketone (1), thus formed, was distilled off and then methylated with methyl iodide

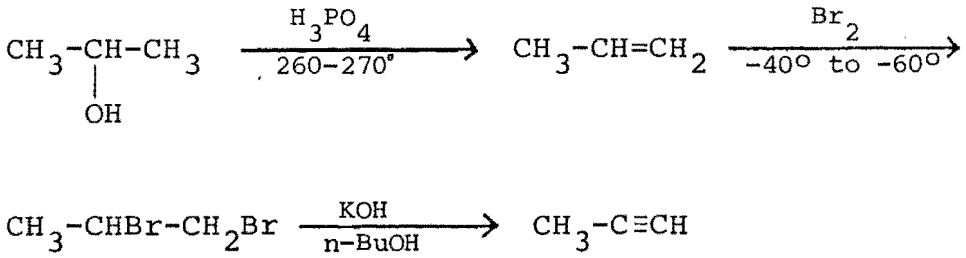
catalyzed by silver oxide to give a 54% yield of methoxyketone (2) which could be separated from the unreacted hydroxyketone (1) by chromatography on 5% deactivated alumina. The methoxyketone (2) had previously been prepared by Temnikova et al.[30] by treating ω-bromopivalophenone (3) with sodium methylate from which they obtained a 35-40% yield of the ketone. Unfortunately this reaction was accompanied by a side reaction which produced the methyl benzoate and isobutylene. Therefore the former method



was adopted[31] for the methylation of hydroxyketone (1) and found to work satisfactorily. It had also been tested on reducing carbohydrates[32] in which the hydroxyl groups could be completely methylated in a single step in good yields using the same reagents in dimethylformamide. The ability of dimethylformamide to accelerate certain alkylation reactions is well established.[33]

Reaction of propyne with freshly-prepared n-butyllithium gave the required propynyllithium. n-Butyllithium was obtained by adding lithium pieces to a solution of n-butyl bromide in ether at -20^{o} with stirring. The concentration of n-butyllithium was determined by titrating two aliquots of the solution with standard hydrochloric acid (1M). The first titration was carried out after the

solution has been hydrolysed with distilled water and this determined the total alkali content. To the second aliquot was added benzyl chloride, and was then hydrolysed with distilled water and titrated. This determined the alkali present other than the n-butyllithium. Difference between the two titration values represented the concentration of n-butyllithium. The production of propyne is outlined below in which dehydration of isopropanol at 260^{o}-270^{o}



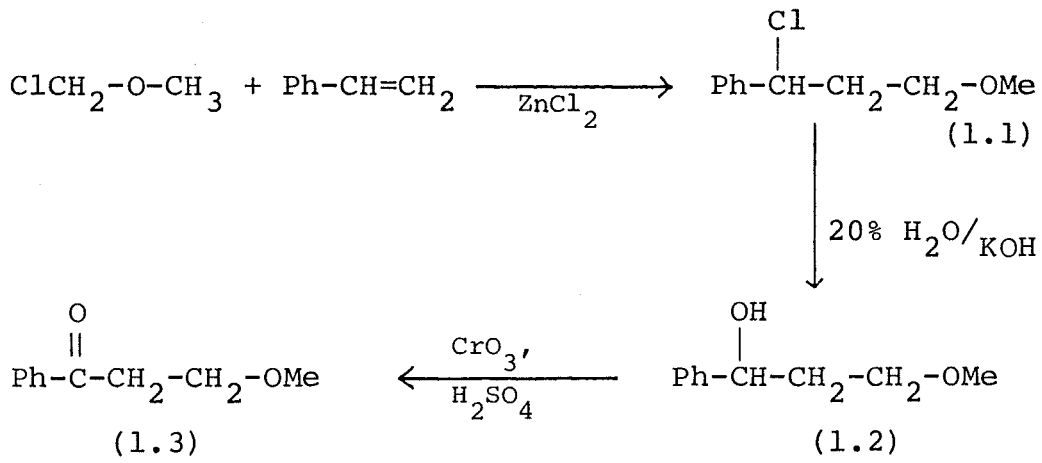
Scheme 13

by phosphoric acid gave propene, followed by bromination to give the propylene bromide which was distilled off as a colourless liquid. On addition of the propylene bromide to a solution of potassium hydroxide in n-butanol with rapid stirring produced a good yield of propyne gas which was collected in a trap immersed in an isopropanol/dry ice bath.

The reaction of propynyllithium with 1-methoxy-2,2-dimethyl-3-phenylpropan-3-one (2) gave a high yield of alkynol (B7) (97%), which was purified by chromatography on 5% deactivated alumina.

1-Methoxy-3-phenylhex-4-yn-3-ol (B4)

The preparation of alkynol (B4) required the precursor, 1-methoxy-3-phenylpropan-3-one (1.3), which was synthesized through a series of reaction steps given in the scheme below.



Scheme 14

Starting from the reaction of styrene and α-chloromethyl methyl ether, it gave the 1-methoxy-3-chloro-3-phenylpropane (1.1)[24] which was distilled off as an oily liquid with a pleasant ethereal odour. The yield of the methoxychloride (1.1)(69%) was satisfactory. Conversion of it into the hydroxymethoxy compound (1.2) was a simple one-step process of hydrolysis with aqueous potassium hydroxide[25]. Fractional distillation gave 80% yield of the hydroxymethoxy compound (1.2), which was then oxidized to the methoxyketone (1.3) by a procedure based on the Jones modification of chromic acid oxidations[26]. The reaction of propynylmagnesium bromide with the methoxyketone (1.3) in tetrahydrofuran gave a high yield of 1-methoxy-3-phenylhex-4-yn-3-ol (B4) which was distilled off as an oil. The same reaction in diethyl ether as solvent did not give a satisfactory yield.

Reactions of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7)

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol with lithium aluminium hydride (1.1 mole) in diethyl ether at 35° for 16 h with stirring gave a crude product from which 1-methoxy-2,2-dimethyl-3-phenylhexa-3,4-diene (C4)

and (E)-1-methoxy-2,2-dimethyl-3-phenylhex-4-en-3-ol (C3) were separated by chromatography on deactivated alumina (see Table 1 for yield data).* The products were identified through their spectroscopic data.

The absorption band at 1965 cm^{-1} in the infrared spectrum of allene (C4) revealed the presence of the allenic function. In the ^{1}H n.m.r. spectrum of (C4) the vinylic methyl protons appeared as a doublet centred at δ1.67 with coupling to the C5-proton (J 8 Hz), itself a quartet centred at δ5.09.

The alkenol (C3) exhibited infrared spectrum absorptions at 3500 and 970 cm^{-1}, which was consistent with its assignment as an alcohol with a trans-disubstituted double bond. The C6-H_3 appeared as a doublet, in its n.m.r. spectrum, centred at δ1.74 with coupling to the C5-proton (J 6Hz). The C5-proton signal, centred at δ5.82, appeared as an overlapping doublet of quartets, with coupling to the C6-H_3 (J 6 Hz) and to the C4-proton (J 14 Hz) itself a doublet (J 14 Hz) centred at δ6.16. On irradiation at the C6-H_3 signal (δ1.74) the C5-proton signal (δ5.82) reduced to a doublet (J 14 Hz).

When deuterium oxide was used to quench the above reaction the relative yields of the allene (C4) and alkenol (C3) were similar. The ^{1}H n.m.r. spectrum of the allene was identical with that above, but the ^{1}H n.m.r. spectrum of the alkenol (C3) revealed a mixture of the 4-deutero and 5-deutero structures. The major component had the 5-deutero structure. For this isomer the C4-proton appeared as a multiplet ($W_{h/2}$ 6 Hz) centred at δ6.17, and the C6-H_3

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* All tables as foldouts at end of thesis.

group gave rise to a broadened singlet at δ1.75. For the 4-deutero isomer the C6-H_3 group appeared as a doublet (J 7 Hz) centred at δ1.73, while the C5-proton gave rise to a quartet (J 7 Hz) centred at 5.79, each component of which was broadened. The 4-deutero/5-deutero isomeric ratio (5:27) was measured from a comparison of the peak intensities of the protonated alkene-carbons in its repetitive-pulse, Fourier-transform ^{13}C n.m.r. spectrum.

On reduction of the alkynol (B7) with lithium aluminium deuteride, under the above reaction conditions, similar yields of the allene (C4) and alkenol (C3) were obtained. The n.m.r. spectrum of the 5-deutero allene (C4) showed no signal in the δ4.5-5.5 region as expected, and the C6-H_3 signal at 1.65 was a singlet indicating deuterium substitution at C5. The n.m.r. spectrum of the monodeuterated alkenol (C3) indicated a mixture of the 4-deutero and 5-deutero isomers in the ratio (23:3) as determined from its ^{13}C n.m.r. spectrum.

When the reaction of alkynol (B7) with lithium aluminium hydride was carried out in tetrahydrofuran, under exactly the same conditions as above, the composition of the two products (C4) and (C3) were formed in a reverse ratio (~1:3) as compared with the ratios obtained from the diethyl ether reactions. Similar product ratios were obtained whether the reaction was worked-up with deuterium oxide, or when lithium aluminium deuteride was employed instead of lithium aluminium hydride. The ratios of the 4-deutero and 5-deutero isomers from the latter two reactions were 49:26 and 30:41 respectively. Increasing

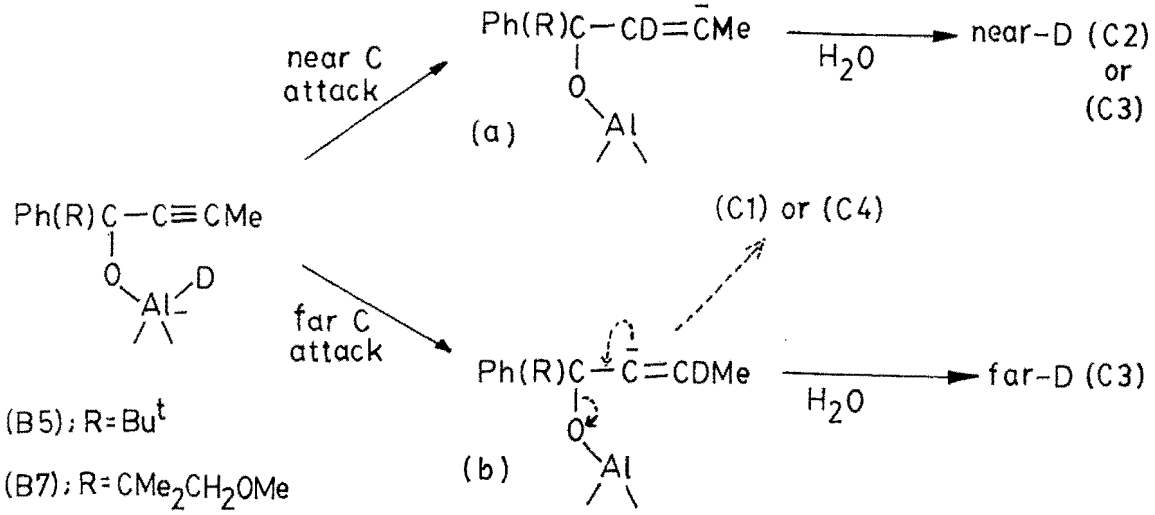
the temperatures of the above reactions to 65° gave a slightly higher yield of allene in each case. In the lithium aluminium deuteride reaction the C4 and C5 deuterated alkenols ratio was 24:16 whilst the reaction with lithium aluminium hydride quenched by deuterium oxide gave a ratio of 15:20.

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol with lithium aluminium deuteride in 2,5-dimethyltetrahydrofuran at 35° for 16 h gave the allene (C4) and alkenol (C3) with a similar product ratio to that obtained from the tetrahydrofuran reaction at a higher temperature, 65°. The 4-deutero and 5-deutero alkenols ratio (25:17) was also similar (cf. 24:16), entries 9 and 7. When the same reaction was carried out at 65° for 2.5 h a higher yield of allene (67%) was obtained and the 4-deutero/5-deutero ratio (23:7) of E-alkenol (C3) indicated a decrease in the yield of the 5-deutero structure (cf. 25:17). Finally, at 91°, and with a reduced reaction time (0.5 h), more allene (75%) was produced and the (E)-alkenol (C3) formed was shown (n.m.r.) to be deuterated specifically at C4. The increasing yield of the allene (C4) as the temperature increased from 35°, 65° to 91° was accompanied by a corresponding decrease in the yield of the alkenol (C3).

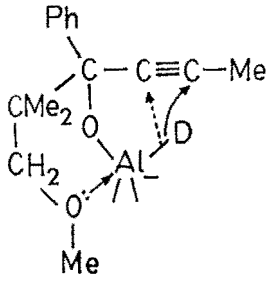
A comparative study of the reactions of alkynol (B7) and 2,2-dimethyl-3-phenylhex-4-yn-3-ol (B5)[20] is necessary to further illuminate the mechanism of the hydride reduction of propargyl alcohols. A summary of the reaction results of alkynol (B5) are given in Table 2. Reaction of the alkynol (B5) with lithium aluminium deuteride in diethyl

ether at 35° for 89 h gave exclusively the 2,2-dimethyl-3-phenylhexa-4,5-diene (C1). However, the same reaction in tetrahydrofuran afforded another product, the (E)-2,2-dimethyl-3-phenylhex-4-en-3-ol (C2) which was specifically deuterated at C4 and predominated to a ratio of 2:1. When the temperature was raised to 65° the relative % yields of allene (C1) and (E)-alkenol (C2) were 66 and 18 respectively. Reaction of the alkynol (B5) in 2,5-dimethyl-tetrahydrofuran at 65° gave essentially the allene (C1) (92%), and the (E)-alkenol (C2)(2%) as the minor product.

For the alkynol (B5) the relative yields of products (C1) and (C2) and the site of initial hydride (or deuteride) attack on the acetylenic system were both markedly solvent-dependent and, in the case of tetrahydrofuran both varied also with the reaction temperature. In contrast, for the reactions of alkynol (B7), while the relative yields of allene (C4) and alkenol (C3) are solvent- and temperature-dependent, the relative yields of products derived from near- and far-carbon deuteride attack are independent of both solvent and reaction temperature. This implies that in the reaction medium the relative amounts of carbanion (a) and (b) produced remained almost constant in every reaction, see Scheme 15. These remarkable results are interpreted in terms of internal solvation of the aluminium atom by the methoxy-substituent in the reacting alkynyloxyaluminium deuteride (4). For alkynol (B5), in the absence of an internal ether, an external and potentially variable ether solvent molecule solvates the aluminium, and thus



Scheme 15



(4)

was responsible for altering the relative amounts of carbanion (a) and (b) which may be formed.

In the reduction of propargyl alcohols by lithium aluminium hydride it is believed that only one ether solvent molecule is needed to solvate the aluminium forming a five-coordinated aluminium species prior to hydride donation to the acetylenic linkage. The above study of alkynol (B7) gives support to this hypothesis. With the involvement of two solvent molecules we might expect a change in the near:far hydride attack ratio as the involvement of a variable ether molecule would place a variable influence in the directing power of the alkoxy-aluminium hydride species. However, the involvement of a

second ether molecule cannot be rigorously excluded, since the stereochemical constraints introduced by the first intramolecular solvation of the aluminium atom may be such that little flexibility remains; the reaction would then be insensitive to changes in the second ether molecule. From the results given in Table 1 there is evidence indicative of the latter postulate. Considering the reactions of alkynol (B7) in three different solvents, diethyl ether, tetrahydrofuran (THF) and 2,5-dimethyl-THF, at 35^{o} for 16 h, a definite solvent effect was observed which could be that due to the second variable ether molecule.

Lithium aluminium hydride reduction of alkynols in a non-ether solvent such as benzene would be expected to give little or no reaction at all. However, the reaction of alkynol (B7) in refluxing benzene for 1 h gave a crude product from which the allene (C4) and (E)-alkenol (C3) were isolated. A substantial reaction was obtained when the reaction was increased to 20 h.

Reactions of 1-methoxy-3-phenylhex-4-yn-3-ol (B4)

Lithium aluminium hydride reduction of alkynol (B4) in diethyl ether at 35^{o} for 2.75 h gave a crude product from which an unidentified compound and the (E)-1-methoxy-3-phenylhex-4-en-3-ol (C6) were isolated, see Table 4 for yield data. The (E)-alkenol (C6) was identified through its spectroscopic data. Its infrared spectrum gave absorptions at 3500 and 970 cm^{-1} which revealed it to be an alcohol with a trans-disubstituted double bond. The vinylic region in

in the ^{1}H n.m.r. spectrum seemed to be part of a degenerated ABX_3 system. It showed only two lines of equal intensity, ca. 2 Hz apart, with satellites on both sides. H4 and H5 were coupled to each other with a coupling constant ca. 16 Hz, derived from a computer simulation of the AB portion of the spectrum. The C6-H_3 appeared as a doublet, with overlapping multiplets in between, centred at δ1.66 with coupling to the C5-proton (J 5 Hz) and C4-proton (J ?). On irradiation at the centre of the AB_q region, the C6-H_3 signal became a singlet centred at δ1.66. Similarly, when irradiated at the C6-H_3 signal the AB_q reduced to a singlet centred at δ5.63. The accurate mass of the parent ion gave a molecular formula $C_{13}H_{18}O_2$.

The unidentified compound was later proved to be the unstable allene (C5) through its spectroscopic data[34]. During the dilution study sufficient allene (C5) was isolated and its ^{1}H n.m.r. spectrum was immediately obtained. After a short lapse of time the ^{1}H n.m.r. spectrum of the decomposed allene was again obtained and was found to be identical with that of the unidentified compound. The accurate mass of the parent ion of the 6-deutero allene (C5) gave a molecular formula $C_{13}H_{15}O_1D_1$.

In using lithium aluminium deuteride for the reduction of alkynol (B4) as above, again the unstable allene (C5) was obtained in addition to the (E)-alkenol (C6) in similar yields. The ^{13}C n.m.r. spectrum of alkenol (C6) revealed it to be a mixture of 4-deutero and 5-deutero isomers having a ratio of 48:25. In the ^{1}H n.m.r. spectrum both the

C4-proton and C5-proton signals of the 5-deutero and 4-deutero isomers appeared as a multiplet ($W_{h/2}$ 8 Hz) centred at δ5.63. The C6-H_3 signal of the 4-deutero structure appeared as a doublet, with a little broadening at the base of the peaks, centred at δ1.68 with coupling to the C5-proton (J 6 Hz). For the 5-deutero isomer the C6-H_3 signal appeared to be a singlet centred at δ1.68. The unstable 6-deutero allene (C5) was confirmed by a comparison of its n.m.r. spectrum with that obtained from a decomposed genuine 6-deutero allene (C5).

Reduction of the alkynol (B4) with lithium aluminium hydride in tetrahydrofuran at 20° for 1 h gave 57% reaction from which only the (E)-alkenol (C6) was isolated and identified. Using lithium aluminium deuteride as reducing agent and extending the reaction time to 3 h, a 100% reaction was obtained and the (E)-alkenol (C6) was isolated as a mixture (53:27) of 4-deutero and 5-deutero isomers. In each of the above two reactions, two other minor products were also isolated by chromatography but their structures could not be identified.

A comparative study of the reactions of alkynol (B4) with those of 2-phenylpent-3-yn-2-ol (B6)[18], of a similar structure, is desirable in further exploring the solvent effect inherent in the reduction of propargyl alcohols with lithium aluminium hydride. Reaction of the alkynol (B6) in diethyl ether with lithium aluminium deuteride at 35° for 44 h gave three products; the 4-deutero allene (C9), the 3-deutero (E)- and (Z)- alkenols (C10 and C11). In tetrahydrofuran as solvent, at 35° and for 44 h, only the

3-deutero (E)-alkenol (C10) was isolated, see Table 3 for yield data.

In the reactions of alkynols (B4 and B6) the product ratios varied with the change of solvent from diethyl ether to tetrahydrofuran. The products which arose by deuteride attack at the near carbon of the acetylenic bond were 48% in both cases when diethyl ether was the solvent. For alkynol (B6) the products formed by deuteride attack at the far-alkyne carbon were slightly higher, by 16%, because a higher yield of allene (C9) was formed. In changing the solvent from diethyl ether to tetrahydrofuran a drastic shift of deuteride attack occurred in the reaction of alkynol (B6), in which the deuteride attacked specifically at the near-alkyne carbon whereas, for alkynol (B4) far-alkyne carbon attack decreased by only 8%. An expected constant overall near:far ratio of deuteride attack for alkynol (B4) was not obtained. This may be due to some side reactions giving rise to the unidentified compounds isolated. Nevertheless, it is envisaged that the methoxy substituent of alkynol (B4) must have played its part in solvating the aluminium atom of the alkynyloxyaluminium hydride and consequently in maintaining the relative amount of carbanion formed by near-carbon attack.

Reaction of 1-methoxy-3-phenylhex-4-yn-3-ol (B4) with lithium aluminium hydride in tetrahydrofuran at a higher temperature, 65^{o}, for 4 h gave a crude product from which two unexpected compounds (C8) and (C7) were isolated in addition to (E)-alkenol (C6) and a few other unidentified compounds. The products (C8) and (C7) were identified

through their spectroscopic data.

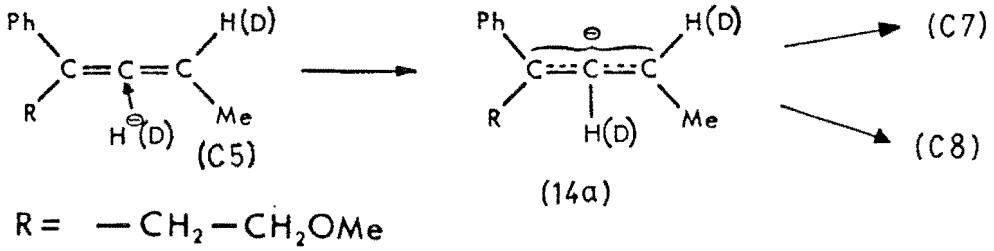
The cyclopropane derivative (C8) exhibited infrared spectrum absorption at 970 cm^{-1}, which was consistent with its assignment as a compound having a trans-disubstituted double bond. In its ^1H n.m.r. spectrum, the C2-proton appeared as an overlapping doublet of quartets centred at δ4.96 with coupling to the C1-proton (J 16 Hz) itself a doublet centred at δ5.28, and to the C3-H_3 (J 5 Hz) itself a doublet centred at δ1.58. The cyclopropane compound (C8) had an ultraviolet maximum at 209 nm (ε8370) [cf. phenylcyclopropane[50] 220(8400)].

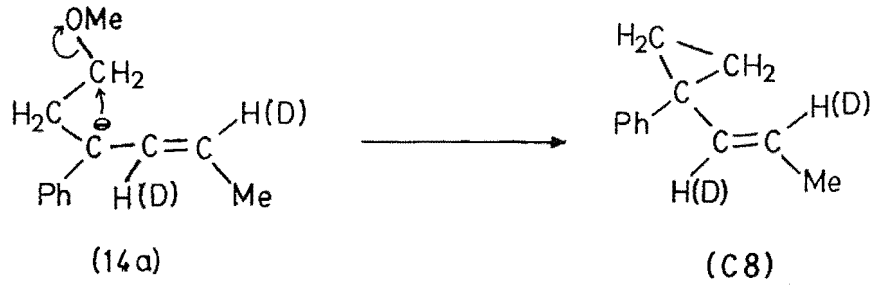
The dimer (C7) had a strong absorption band at 1600 cm^{-1} in its infrared spectrum which was characteristic of a diene. In its ^1H n.m.r. spectrum, the C4-proton signal appeared as a doublet centred at δ5.48 with coupling to the C5-proton (J 10 Hz), itself a doublet of quartets centred at δ3.47 with additional coupling to the C5-CH_3 (J 7 Hz). The C7-proton signal appeared as a quartet centred at δ5.67 with coupling to the C7-CH_3 (J 7 Hz), itself a doublet centred at δ1.75. C5-CH_3 signal appeared as a doublet overlapping with the cyclopropane protons signal, centred at δ1.13.

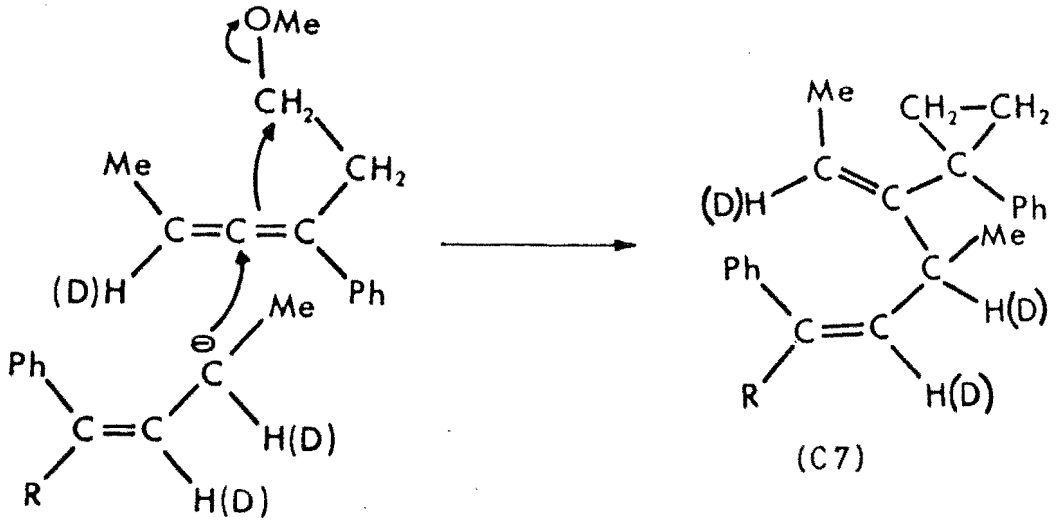
Reduction of alkynol (B4) with lithium aluminium deuteride as above, but with an extended reaction time (17 h), gave similar yields of (E)-alkenol (C6) and the two cyclopropane derivatives (C7 and C8). The ^1H n.m.r. spectrum of the monodeuterated (E)-alkenol (C6) was consistent only with a 4-deutero structure. The ^1H n.m.r. spectrum of the 1,2-dideutero cyclopropane derivative (C8) showed no signal in the δ5-6 region, and the C3-H_3 signal collapsed to a

singlet centred at δ1.57. In the ^1H n.m.r. spectrum of the dimer (C7) the signals centred at δ5.48, 3.47, 5.67 were absent; the C5-CH_3 and C7-CH_3 gave rise to two singlets centred at δ1.13 and 1.73 respectively; thus indicating substitutions by deuterium at the 4-, 5- and 7-positions.

The extent and location of deuterium labelling in compounds (C7) and (C8) from the lithium aluminium deuteride reaction are consistent with their formation via deuteride ion attack on the intermediate deuteroallene (C5), followed by reactions of the delocalised carbanion (14a), Scheme 16. Internal displacement of methoxide ion from carbanion (14a)



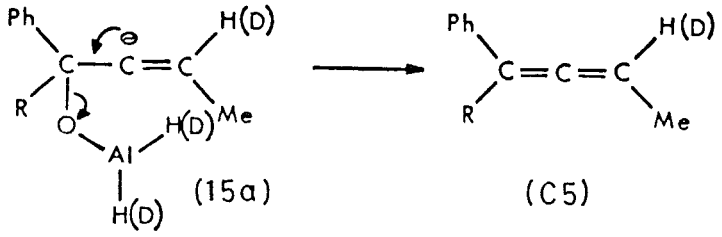




Scheme 16

would yield the cyclopropane derivative (C8), while the dimer (C7) could be formed by intermolecular attack of carbanion (14a) on a second deuteroallene (C5), again with the loss of a methoxide ion.

In more dilute solution (10 times the normal volume of tetrahydrofuran was used) the relative yield of dimer (C7) was sharply reduced consistent with an intermolecular mechanism, and the unstable allene (C5) was isolated. The higher yield of 5-deutero (E)-alkenol (C6), which arises by deuteride attack at C5, was a reflection of incomplete conversion of carbanion (15a) into deutero allene (C5) prior to reaction quenching.



(15a) (C5)

By inspection of Table 4 it is interesting to note that the percentage of near-carbon attack was constant (~49%)* in all the reactions, even though the anticipated constant near:far overall ratio was not attained. However, it seems likely that this feature of these reactions is the result of the conversion of the carbanion arising from far-carbon attack into products not accounted for in the near:far ratio listed. Coupled with the evidence from the reactions of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7), it can be concluded that the implicit constant value of the near:far ratio was again the result of an internal solvation of the aluminium atom by the methoxy-substituent.

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* Average value taken.

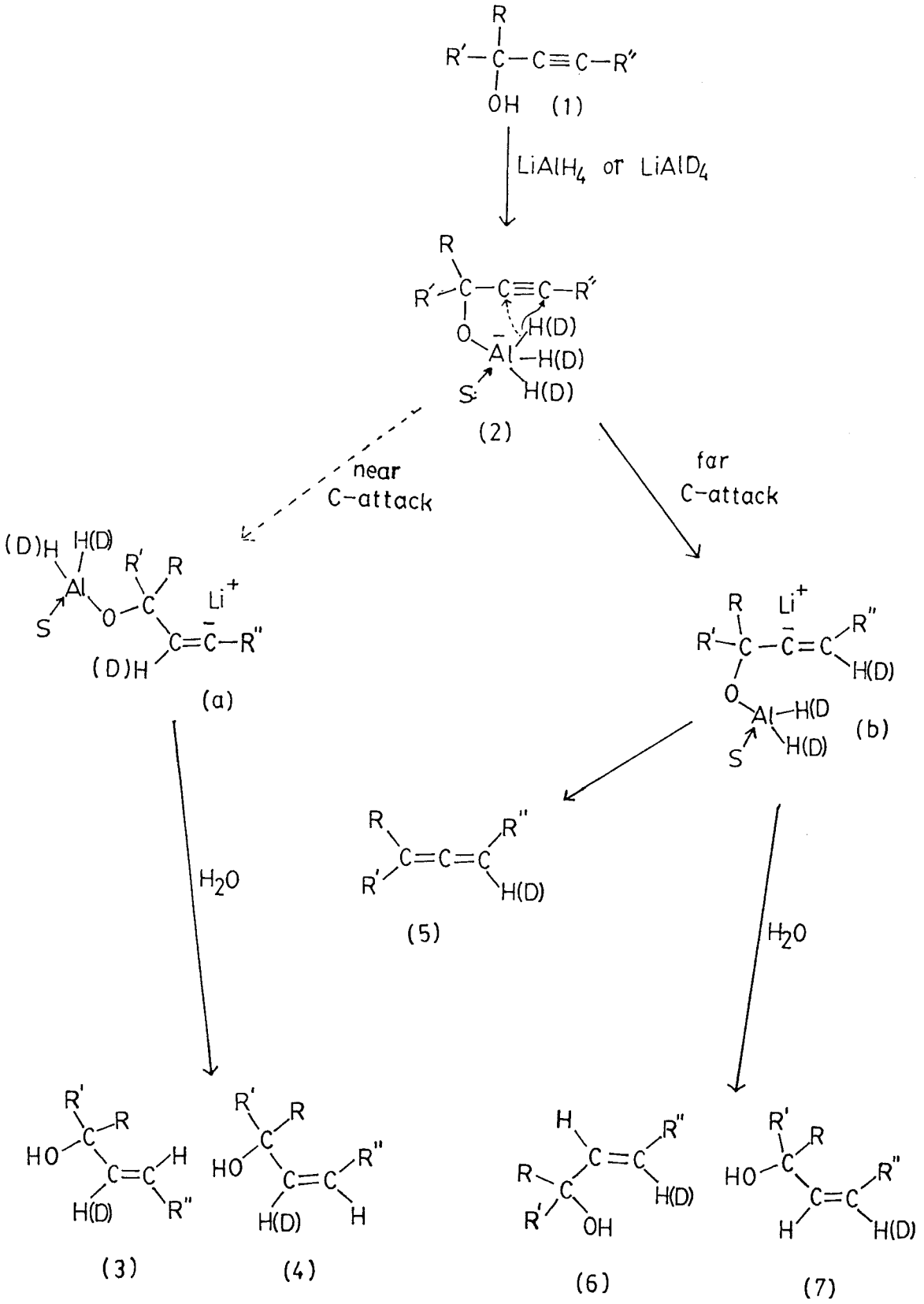
PART II STRUCTURAL EFFECTS AND REACTIONS OF 4-TERT-BUTYL-1-PROPYNYLCYCLOHEXANOLS.

(a) Introduction.

In Part I it has been demonstrated that an ether solvent molecule has the directing power on the alkoxy-aluminium hydride group, and is therefore a deciding factor between the two reaction pathways leading to carbanions (a) and (b), Scheme (17). It is now necessary to introduce another factor, the structural effect of the alkynol, which may have an influence on the partitioning between these two reaction pathways.

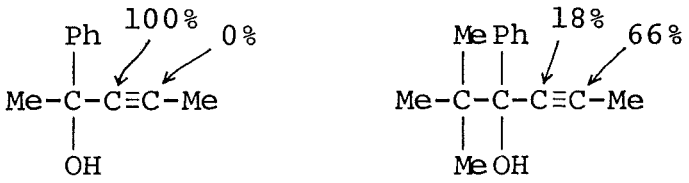
Referring to the structure of alkynol (1) in Scheme (17), it is notable that hydride attack at the near carbon will be favoured if R'' is an electron withdrawing group which is capable of stabilizing carbanion (a). Thus, in the reduction of 2,2-dimethyl-5-phenylpent-4-yn-3-ol[12] (A7, Block A) in either tetrahydrofuran or diethyl ether as solvent the sole site of hydride attack is at the near carbon of the alkyne function, the carbanionic centre being stabilized by the adjacent phenyl group; no parallel stabilization is possible in carbanion (b).

When, however, R'' is a group which is not able to stabilize an adjacent carbanion, then there will be no marked bias in favour of one or other of the two carbanion-forming reaction pathways and products from both carbanions may be anticipated. Apparently, the greater the steric


LiAlH4 or LiAlD4
near C-attack
far C-attack
H2O
H2O
(1)
(2)
(a)
(b)
(3)
(4)
(5)
(6)
(7)

Scheme 17

size of R and R′ the more favoured is hydride attack at the far carbon of the alkyne system. This is understandable as the alkynyloxyaluminium hydride group (2) is being pushed further towards the far carbon. For example, it has been shown that reduction of 2-phenylpent-3-yn-2-ol[18] (S, see diagram below) with lithium aluminium hydride in tetrahydrofuran as solvent gave only the trans-alkenol which arose by hydride donation to the near carbon, whereas in the same solvent 2,2-dimethyl-3-phenylhex-4-yn-3-ol(T)[20] gave 66% allene, which can only be formed by hydride attack at the far carbon and 18% trans-alkenol formed where the attack of hydride is at near carbon. Thus, the replacement of the methyl group by a more bulky tertiary butyl group increases the far carbon attack significantly (0 → 66%).



(S) (T)

In order to examine in more detail the steric effect of R and R′ a series of eight substituted 4-tert-butylcyclohexynols were synthesized and their reactions with lithium aluminium hydride in a range of ether solvents were studied. The structural diagrams of the alkynols (B8),(B9),(B10),(B11),(B12),(B13),(B14) and (B15) are summarized in Block B.

(b) Discussion.

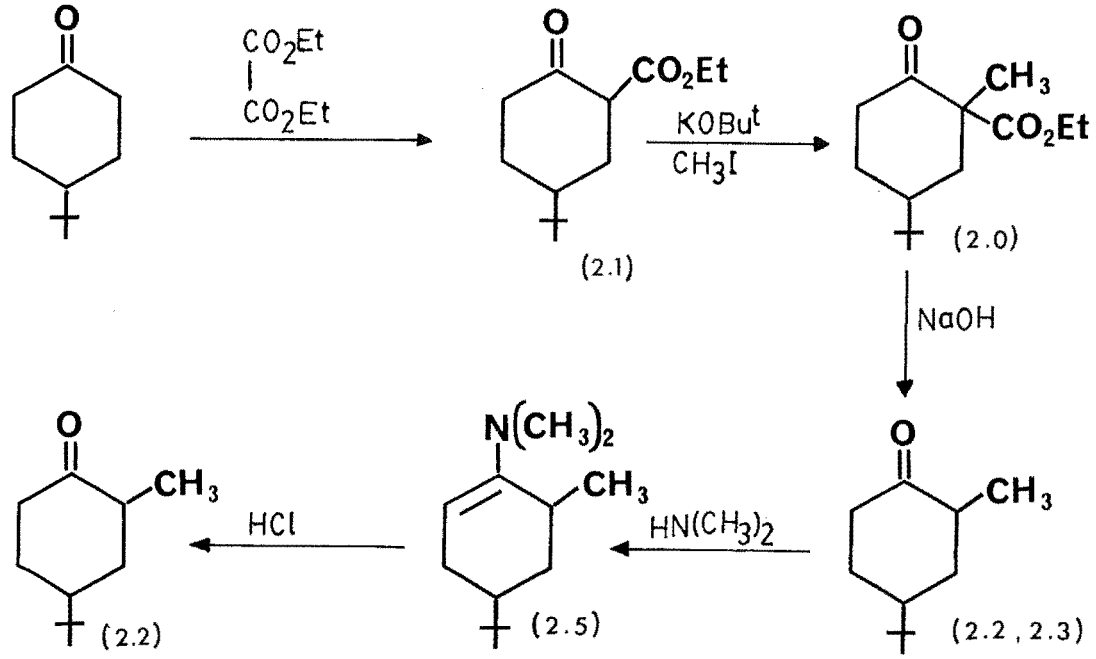
4-α-t-Butyl-1-β-propynyl- and 4-α-t-butyl-1-α-propynyl-cyclohexan-1-ols (B8 and B11).

The reaction of 4-t-butyclcyclohexanone with propynyl-magnesium bromide (prepared by bubbling propyne into a freshly-made solution of ethylmagnesium bromide in ether) gave a mixture of the isomeric alkynols (B8 and B11), which could be separated by chromatography on deactivated alumina. The ratio of the epimers (B8 and B11) obtained by this method of preparation was 17:38 respectively. In agreement with its assigned configuration the hydroxyl proton and C1 signals of alkynol (B11) with its hydroxyl group in the equatorial position, appeared at a lower field[35,36] in its ^{1}H and ^{13}C n.m.r. spectra than those of alkynol (B8) respectively. This criterion for ^{1}H spectra, however, is not always found to be reliable[37]. A Lanthanide Induced Shift (LIS) technique was therefore applied to both of the isomers to confirm the individual assignment, see Appendix. In this experimental technique the bound or limiting shifts (Δ_1) of a set of ^{13}C n.m.r. signals were extrapolated from a plot of the observed induced shifts (Δ) versus the molar ratio of reagent to substrate ($^{L_o}/S_o$) present in solution. A comparison of the Δ_1 values of alkynols (B8 and B11) was sufficient to demonstrate the substrate topology in each case. Unfortunately, it was not possible to gather any information from the observed induced shifts from the ^{1}H n.m.r. signals due to broadening of the unresolved peaks. It was found that for the above isomeric alkynols and for

alkynols (B9 and B12, B10 and B13), the isomer with the hydroxyl group in the axial position is less polar, and thus was eluted first from an alumina column[51].

2-α-Methyl-4-α-t-butyl-1-β-propynyl- and 2-α-methyl-4-α-t-butyl-1-α-propynyl- cyclohexan-1-ols (B9 and B12).

The synthesis of alkynols (B9 and B12) required a pure sample of cis-2-methyl-4-t-butyl-1-cyclohexanone (2.2) which could be conveniently prepared through a series of reactions starting with 4-t-butylcyclohexanone, see reaction Scheme (18) below. 4-t-Butylcyclohexanone was allowed to undergo a Claisen condensation with ethyl oxalate,



Scheme 18

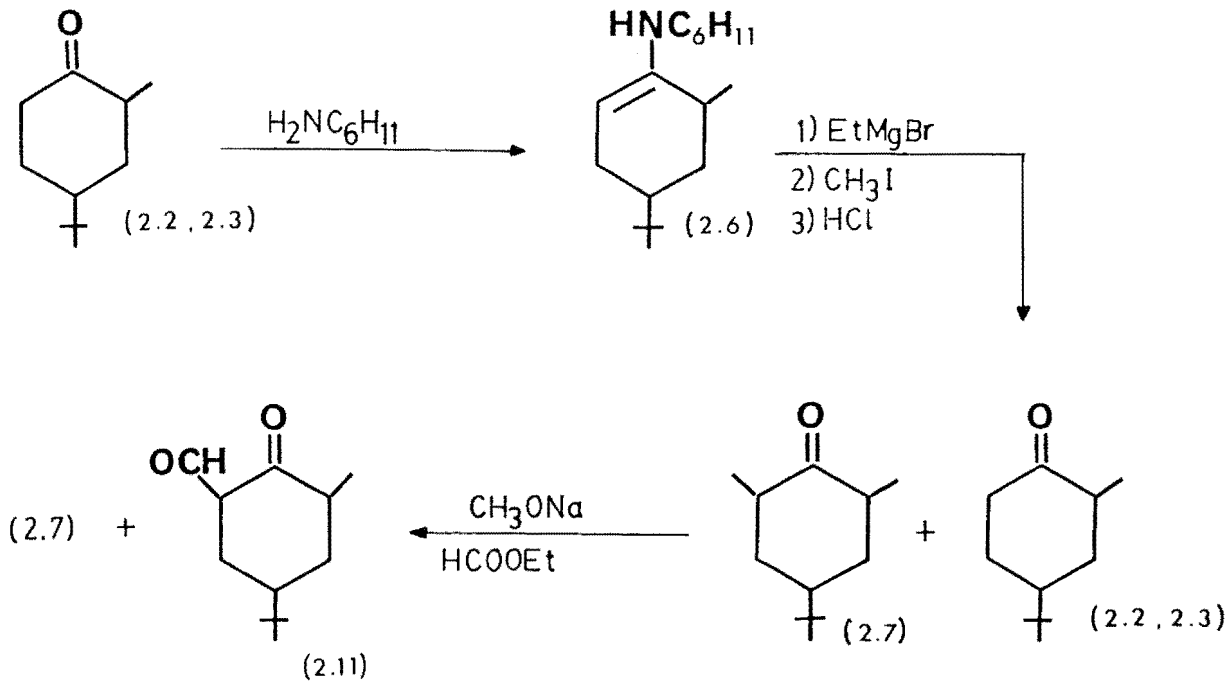
followed by decarbonylation to give ethyl 4-t-butyl-1-cyclohexanone-2-carboxylate (2.1) which was fractionally distilled through a 2 ft Vigreux column as a very pale yellow liquid.

Methylation of keto ester (2.1) with potassium tert-butoxide gave the methylated keto ester (2.0) in a 93% yield, which was hydrolysed and decarboxylated to give a mixture of the cis- and trans-2-methyl-4-t-butyl-1-cyclohexanones (2.2 and 2.3), believed to be in the ratio of about 93:7[28,38]. The yield of (2.2 and 2.3) was 96% which was slightly higher than the literature yield[28] of 91%. An enamine synthesis of the mixture of ketones (2.2 and 2.3) with dimethylamine in the presence of titanium tetrachloride led to the isolation of a 51% yield of N,N-dimethyl-N-(2-methyl-4-t-butyl-1-cyclohexen-1-yl)amine (2.5). Its hydrolysis gave the pure cis-ketone (2.2).

The cis-ketone (2.2) was brought into reaction with propynyllithium, and the mixture of isomeric alkynols (B9 and B12) formed were separated by chromatography on deactivated alumina. The ratio of B9:B12 was 40:60. Thus, the substitution of a methyl group at the C-2 position of the alkynol (B8) caused a substantial relative increase (23%) in the formation of the epimer (B9) with the hydroxyl group in the axial position (see Table 5). Again, in the ^{1}H and ^{13}C n.m.r. spectra, the hydroxyl proton signal and the C-1 signal occurred at lower field in the case of alkynol (B12). To confirm the above configurational assignments the Lanthanide Induced Shift (LIS) technique was again applied to both of the alkynols (B9 and B12). A computational approach on the LIS values was not adopted, as a comparison of the Δ_1 values between the alkynols permitted the identification of the isomers.

2,6-α,α-Dimethyl-4-α-t-butyl-1-β-propynyl- and 2,6-α,α-dimethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ols (B10 and B13).

The preparation of 2,6-dimethyl-4-t-butyl-1-cyclohexanone (2.7) followed the reaction sequence outlined below. The mixture of isomeric ketones (2.2,2.3) which has been prepared, as before, was brought into reaction with cyclohexylamine in the presence of p-toluenesulfonic acid. The enamine (2.6) which was isolated by distillation was treated with ethyl magnesium bromide followed by methylation with methyl iodide, and subsequent hydrolysis gave a mixture of the unreacted ketones (2.2,2.3) and the wanted dimethyl ketone (2.7). To separate these ketones, the mixture of



Scheme 19

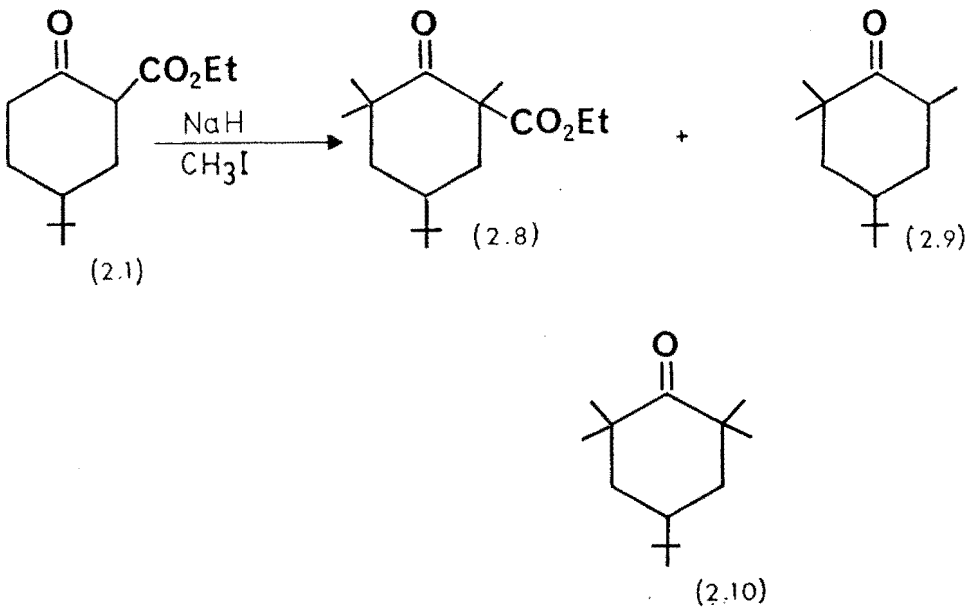
these compounds was treated with ethyl formate. The preferential formation of 6-formyl-2-methyl-4-t-butyl-1-cyclohexanone (2.11) allowed an easy separation, as it

was highly soluble in the aqueous phase, and extraction with benzene gave pure ketone (2.7).

Reaction of propynyllithium with the dimethyl ketone (2.7) led to a mixture of isomeric alkynols (B10 and B13) in the ratio 65:35 respectively. As shown in Table 5, for the alkynol (B10), the C-1 signal and the hydroxyl proton signal of its n.m.r. spectra were at a higher field than the corresponding signals of the other epimer (B13), and therefore the alkynol (B10) was assigned as the epimer with the hydroxyl group in the axial position. In the ^{13}C n.m.r. spectrum of each isomer, ten peaks were observed which indicated a symmetry across each compound. This showed that the two methyl groups at C-2 and C-6 positions must occupy either the equatorial or the axial positions. On steric ground, the former was preferred in the preparation of its precusor ketone (2.7) from the enamines (2.6). Further confirmation of their configurations at C-1 was obtained from the lanthanide shift work, see appendix.

2,2,(6-α)-Trimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol(B14).

The required trimethyl ketone (2.9) was synthesized according to the reaction steps outlined below. Exhaustive methylation of the keto ester (2.1) gave the trimethyl keto ester (2.8) in addition to the trimethyl and tetramethyl ketones (2.9 and 2.10) which were formed by partial elimination of the ester group. The trimethyl keto ester (2.8), isolated by spinning-band distillation was subjected to acid hydrolysis under stringent conditions, and decarboxylation of the



Scheme 20

reaction product led to pure ketone (2.9), without the initial compound (2.8) as impurity.

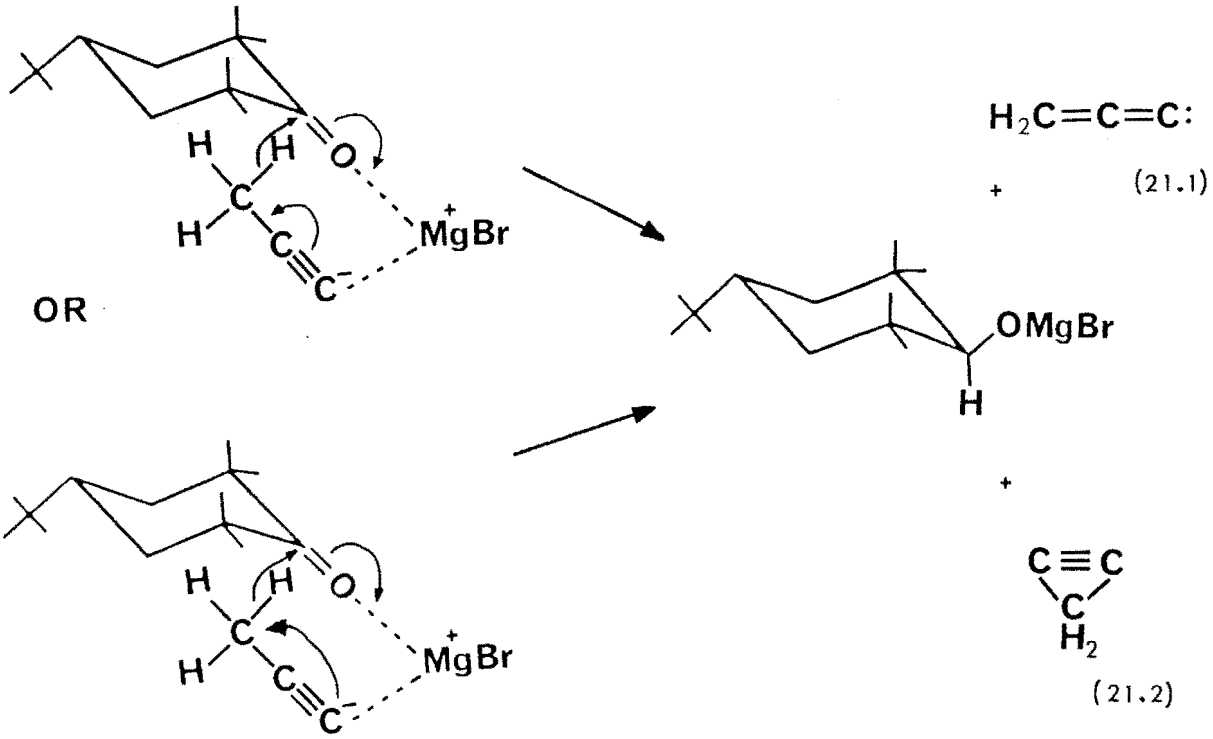
Reaction of the trimethyl ketone (2.9) with propynylmagnesium bromide led exclusively to one of the isomeric alkynols, (B14), with the hydroxyl function in the equatorial position. Its configurational assignment was not as straightforward as for those alkynols which have already been discussed before since no comparison could be made with the other epimer. However, the value of its C-1 n.m.r. chemical shift as compared with others (see Table 5) suggested that it was an equatorial alcohol. A computational approach on the lanthanide shift values was also desirable in the elucidation of its conformation. In this approach it was shown that the alkynol (B14) has the conformation having its hydroxyl group in the equatorial position.

2,2,6,6-Tetramethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B15).

The 2,2,6-trimethyl-4-t-butyl-1-cyclohexanone (2.9) obtained from the decarboxylation of trimethyl keto ester (2.8) was subjected to further methylation, which lead to a mixture of unreacted ketone (2.9) and the 2,2,6,6-tetramethyl-4-t-butyl-1-cyclohexanone (2.10). The separation of these ketones could be achieved by recrystallisation of the mixture, rich in (2.10), from ethanol/water, which led to the crystalline tetramethyl ketone (2.10).

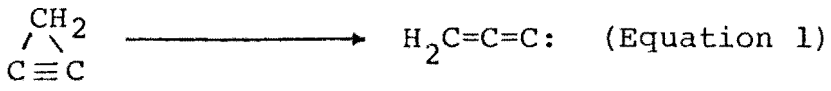
The first attempt to synthesize the alkynol (B15) was to react the Grignard reagent, propynylmagnesium bromide, with the tetramethyl compound (2.10), which led to an unexpected compound (B16) in addition to the alkynol (B15). The ratio of (B16):(B15) was estimated from chromatography of the crude product on alumina to be about 4:1. The structure of (B16) was later proved to be the 2,2,6,6-tetramethyl-4-α-t-butyl-cyclohexan-1-β-ol which could be reproduced by reducing the ketone (2.10) with lithium aluminium hydride. The configuration of the alkynol was again determined by a computational approach to the lanthanide induced shift values.

The formation of the secondary alcohol (B16) from the Grignard reaction was puzzling because the reduction to give the alcohol would imply the transient formation of either one of the two hypothetical species, (21.1) or (21.2). Chapman[48] has demonstrated that cyclopentyne could actually be synthesized and has also speculated that



Scheme 21

both cyclobutyne and cyclopropyne should exist. Quantum mechanical calculations based on Molecular Orbital Theory has recently been applied on the electronic structure of cyclopropyne[39]. Results revealed that triplet cyclopropyne exhibits a true relative minimum in its energy state. Thus it would appear that, at least in principle, triplet cyclopropyne is "makeable". Preliminary theoretical work also raised the possibility that the singlet isomerization to propadienylidene (equation 1) might proceed with no barrier at all.



When the ketone (2.10) was brought into reaction with propynyllithium, not a trace of the alcohol (B16) could

be found, and only one of the isomeric alkynols was formed. It was identified as the epimer (B15) through its spectral data. A computational approach to its lanthanide shift values was applied in the determination of its conformation.

The Stereochemistry of Reaction of substituted cyclohexanones with propynylmagnesium bromide or propynyllithium.

The stereochemical results for the reactions of five substituted 4-t-butylcyclohexanones, involving the spatial addition of the propynyl reagents on either side of the carbonyl group, was summarized in Table 5 and have been briefly mentioned before. In this discussion an attempt was made to explain the experimental data obtained for the reactions of those five cyclic ketones.

The stereochemistry for the reaction of unhindered cyclohexanones with Grignard reagents and with metal hydrides has been explained by Marshall et al [40] on the basis of the relative shielding of a cyclohexylidene carbon atom by α and β substituents (see diagram below).

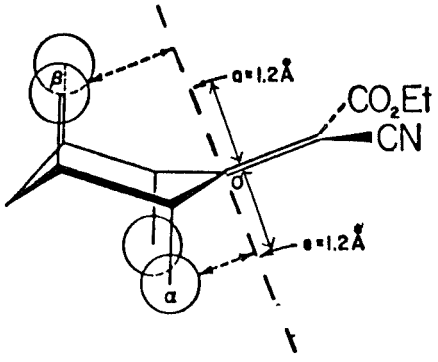


Figure 1

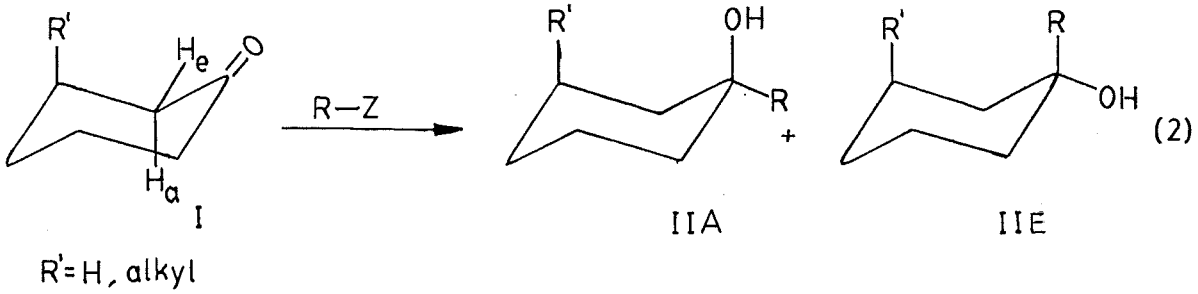
It was postulated that if α and β are identically substituted, attack by the nucleophilic reagent, at the

transition state, will be more effectively blocked by the axial α-group at a short distance from O and more effectively blocked by the axial β-group at a longer distance from O. This was taken to mean that in the case of Grignard reagents, additions must occur at a somewhat greater distance from the carboxyl carbon than analogous additions of hydrides. This would result in greater steric interference by the axial β-substituents and therefore gave more axial alcohols.

A similar argument[41], which is based solely on steric factors has been proposed for the reduction of cyclic ketones by lithium tri-t-butoxyaluminium hydride. Examples have also been drawn on the reduction of 4-t-butycyclohexanone to show that an axial attack (by a small or rod-like substituent, e.g. H^-, -C≡C-H) should be favoured (90:10) over an equatorial attack, due to the greater steric interference by the presence of the axial hydrogens in positions 2 and 6 which hinder attack from the equatorial side. By this argument, an axial methyl group at either position will have a greater influence than an axial hydrogen. This prediction was borne out by the reduction of 4-t-butyl-2,2-dimethylcyclohexanone which gave more axial attack (100%) than its unmethylated analog, 4-t-butylcyclohexanone (89.7%).

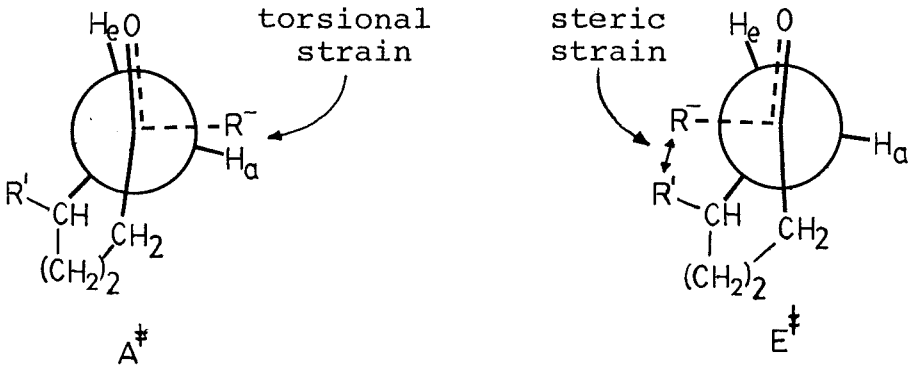
In a more recent paper[42] the steric influence of the axial hydrogens at positions 2 and 6 in cyclohexanones has been interpreted in terms of torsional strain. Two transitional states were postulated for the reactions of cyclohexanones, equation 2, with hydrides (R=H) and with Grignard reagents (R=alkyl). Torsional strain[43] was said

to be involved in the formation of the axial alcohol (IIA)



(2)

("equatorial attack") through a partially eclipsed 'reactant-like'[44] transition state $A^{\ddagger}$, and formation of the equatorial



alcohol (IIE) ("axial attack") implies an essentially staggered transition state $E^{\ddagger}$ involving some degree of steric strain between R^{-} and R′ (axial alkyl group) at the 3 or 5 position. The interplay of these two factors determines the stereochemical outcome of the reactions of cyclohexanones with hydrides and with Grignard reagents.

Results from Table 5 show a proportional increase in the formation of axial alcohols* (equatorial attack) in going from the unmethylated compound to the 2,6-dimethyl ketone (1st 3 entries). These results were contrary to the assumption[41] made on the basis that equatorial ortho** substituents to the carbonyl carbon are situated in the

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* OH group in the axial position.

** The usage of ortho and meta is as in ref. 47.

"plane" of the carbonyl group and will not interfere with a species approaching the carbonyl group either from its axial or equatorial side. Geometrical calculation[46] shows that the projection valency angle between the ortho methyl group and the carbonyl double bond amounts to 15° (105° for an axial arrangement of the methyl group), see figure 2 below. As has already been pointed out[47], the preferred

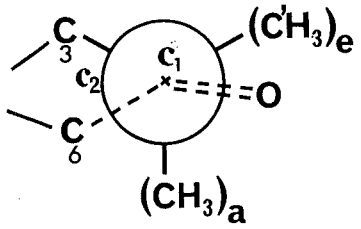

Figure 2

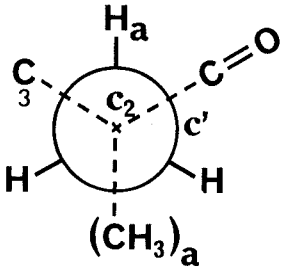

Figure 3

conformation of the methyl group in the equatorial position (figure 3) will have its hydrogen atoms in a skew position with respect to the substituents at C2. In this way, the hydrogen atom (H_a) and the axial meta hydrogen atoms will be at equal distance from the carbon atom C1. That is, there were three axial meta hydrogen atoms for the 2-methyl ketone imposing additional steric hindrance as compared to the unmethylated 4-t-butylcyclohexanone, which resulted in an increase of axial alcohol. For the 2,6-dimethyl ketone there were four axial meta hydrogen atoms which caused a shift to predominant equatorial attack by the propynyl reagent giving more axial alcohol consequently.

Reactions of 2,2,6-trimethyl and 2,2,6,6-tetramethyl 4-t-butylcyclohexanones gave solely the equatorial

alcohols. Although it is conceivable that 2,2,6,6-tetra-methyl-compound (B15) might exist in a skew boat form, because of the syn-axial methyl-methyl interaction there is evidence (see molecular mechanics calculations: Appendix) that the two alcohols (B14), (B15) both exist in the chair form, but with the hydroxyl end of the ring slightly flattened. The axial methyl groups in compound (B15) are therefore further apart than they would normally be in a perfect chair conformation.

Reactions of seven substituted 4-t-butyl-1-propynylcyclohexan-1-ols (B8 to B14), Tables 6 - 12.

The lithium aluminium hydride reduction of 2,6-α,α-dimethyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B10) in refluxing 2,5-dimethyltetrahydrofuran for 6 h gave a crude product from which trans*-allene (D13), 2,6-α,α-dimethyl-4-α-t-butyl-1-β- (Z)- and (E)-propenylcyclohexan-1-ols (D14 and D15) were isolated by chromatography on deactivated alumina (see Table 8 for yield data). The compounds were identified through their spectroscopic data.

For the trans-allene (D13), the characteristic infrared absorption band at 1955 cm^{-1} indicated the presence of the allene function. In its ^{1}H n.m.r. spectrum the C9-H_3 protons appeared as a doublet centred at δ 1.64 with coupling to the vinylic proton (J 7 Hz). The C8- vinylic proton gave rise to a doublet of doublet of quartets centred at δ5.10 with additional long range couplings to the C2- and C6- axial protons (J 3.5 Hz in each case).

The cis- alkenol (D14) exhibited infrared spectrum absorptions at 3500 and 715 cm^{-1}, consistent with its assignment as an alcohol with a cis-disubstituted double bond[49]. In the ^{1}H n.m.r. spectrum of compound (D14) the C7-proton signal appeared as a doublet centred at δ4.99 with coupling to the C8-proton (J 12 Hz) itself an overlapping doublet of quartets centred at δ5.46 with additional

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* 4-t-Butyl and C9-H_3 groups in a trans-relationship.

coupling to the C9-H_3 protons (J 6 Hz), and the C9-H_3 itself appeared as a doublet centred at δ1.82.

The second allylic alcohol (D15) exhibited absorptions at 3525 and 970 cm^{-1} in its infrared spectrum which revealed its nature as an alcohol with a trans-disubstituted double bond. In the ^1H n.m.r. spectrum of (D15) the C9-H_3 signal appeared as a doublet centred at δ1.72 with coupling to the C8-proton (J 6 Hz). The C8-proton signal gave rise to an overlapping doublet of quartets centred at δ5.52 with coupling to the C7-proton (J 16 Hz) and to the C9-H_3 group (as above). The C7-proton appeared as a doublet centred at δ5.18 with coupling to the C8-proton (as above).

When deuterium oxide was used to quench the above reaction instead of water it gave similar yields of allene (D13) and the two alkenols (D14) and (D15). As expected, no deuterium substitution took place in the case of allene (D13) and its ^1H n.m.r. was identical with the above. The ^1H n.m.r. spectrum of each of the two monodeuterated alkenols (D14 and D15) was consistent only with a 8-deutero structure. In the ^1H n.m.r. spectrum of the (Z)-alkenol (D14) no signal was observed in the region around δ5.46 indicating deuterium substitution at C-8. The C7-proton appeared as a broad singlet ($W_{h/2}$ 6 Hz) centred at δ4.98, and the C9-H_3 collapsed to a broadened singlet centred at δ1.82. Similarly, the ^1H n.m.r. spectrum of (E)-alkenol (D15) showed no signal in the region around δ5.52. The C9-H_3 again gave rise to a broadened singlet centred at δ1.70, and the C7-proton appeared as a broad singlet ($W_{h/2}$ 6 Hz) centred at

δ5.15. In the ^{13}C n.m.r. spectrum of (D14) and (D15), only the protonated C-7 signal was detected in each case.

By the above techniques, all the allenic compounds and allylic alcohols which were formed from the reactions of alkynols (B8-14), were identified in like manner. Their yield data are given in Table 6 to Table 12. In the case where the individual allylic alcohols existed as two mono-deuterated species their isomeric ratio was determined from a comparison of the peak intensities of the protonated alkene-carbons in its repetitive-pulse, Fourier-transform ^{13}C n.m.r. spectrum. Unfortunately, some of the allenes (D7), (D10), (D13), (D16) and D(22) decomposed readily before elemental analysis could be obtained. A completely different ^{1}H n.m.r. spectrum could be expected after 24 h from the time of isolation.

A comparative study of the reductions of propargyl alcohols (B8), (B9) and (B10).

This series of alcohols is chosen in order to examine the effects of progressively increasing steric compression on the reactions of alkynols. The common structural feature of these alcohols is that they are all axial alcohols with equatoral acetylenic group in the 1 position.

In the tetrahydrofuran reactions of propargyl alcohols (B9) and (B10), the product ratios of allene: alkenol were essentially the same while the reduction of (B8) in the same solvent gave slightly more alkenol, a mere 10% increase, accompanied by the same amount

of decrease in the allene production. However, their near:far hydride attack ratios do not differ much along the series.

Reactions of the alkynols (B8), (B9) and (B10) with lithium aluminium hydride in refluxing 2,5-dimethyltetrahydrofuran afforded high yields of allene, and in each case cis-alkenol was also formed in addition to the trans-alkenol. Along the series (B8) (B9) (B10) a progressive percentage increase of allene from 70* to 81 to 89 was observed. The trend was reverse for the production of alkenols (Z- and E-) from 19* to 13 to 6 (approx. ratio 3:2:1). For the reduction of compound (B9) an equal amount of the cis- and trans-alkenols were formed while more trans-alkenols than cis- were given by the reactions of compounds (B8) and (B10). There was little difference in the overall near:far ratio for alkynols (B8) and (B9), about 11:80 and 13:81 respectively, but slightly more far-carbon attack was obtained for (B10), its near:far ratio was 6:89.

In diethyl ether as solvent the reactions of alkynols (B8), (B9) and (B10) produced the three compounds:allene, (Z)- and (E)- alkenols. There was a slight increase in allene in going from either (B8) or (B9) to (B10). Again the total alkenols (cis and trans) formed in going from (B8) to (B9) to (B10) followed the same decreasing order as above from 31 to 23 to 11 (approx. ratio 3:2:1). The overall near:far ratio for (B8) and (B9) was not significantly different but for (B10) the effect of increasing

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* An average value was taken.

substitution in the neighbourhood of Cl is becoming apparent with a perceptible trend to greater far-carbon attack.

A comparative study of the reductions of a series of propargyl alcohols (B11), (B12), (B13) and (B14).

This series of alcohols are all equatorial alcohols, with the acetylene groups arranged in the axial positions. By examination of Tables 7 - 12 a few trends can be recognised along the series (B11), (B12), (B13) and (B14).

Reaction of alkynol (B11) with lithium aluminium hydride in refluxing tetrahydrofuran afforded a good yield of the trans-alkenol (D6) with allene (D4) and cis-alkenol (D5) as minor products. In the same solvent, more allene was obtained in the reduction of alkynol (B12) which has a methyl group substituted at the 2 position. In the same reaction conditions, a further rise of allene formation was observed from the reduction of the 2,6-dimethyl analog of compound (B11). The formation of allene now exceeded the (E)-alkenol by ~6%, and no (Z)-alkenol could be detected from the crude product mixture. A greater effect in the reduction of alkynol (B14) should be realized as the three substituted methyl groups would impose serious steric compression on the alkynyloxyaluminium hydride system. Thus, the lithium aluminium hydride (LAH) reaction of substrate (B14) in refluxing tetrahydrofuran gave twice the proportion of allene with respect to the (E)-alkenol. Again, no cis-alkenol was isolated in the reduction of this sterically hindered alcohol. The overall near:far ratios along this

series of compounds (B11), (B12), (B13), (B14) were 79:15, 48:46, 41:54, 27:66 respectively.

The sensitivity on the reduction of this series of compounds to methyl substitution at C2 and C6 was even more pronounced when 2,5-dimethyltetrahydrofuran was the solvent, and this was reflected by the overall near:far ratios which change from (50:36) to (16:80) to (7:88) to (3:91) along the same series of compounds. Allene production progressed from 35 to 80 to 89 to 90. The replacement of a hydrogen atom at the equatorial position by a methyl group caused a sudden increase in allene formation as the reduction of alkynol (B12) showed when compared with alkynol (B11). Increasing steric crowding at the 2 and 6 positions favoured production of allene over the formation of alkenols, as shown by the reactions of alkynols (B13) and (B14). All the alkenols formed in this series of reactions arose from hydride attack at the near carbon atom of the acetylenic system.

In the diethyl ether reactions of substrate (B11) at 35° for different reaction times; 23 h, 45 h and 96 h, there was little difference in the product compositions. The predominant product was the (E)-alkenol, ~80%, with equal proportion of allene and (Z)-alkenol formed when the reaction time was 96 h. All the alkenols were formed from specific hydride attack at the near alkyne-carbon. This specific hydride attack at the near alkyne function was also followed in the diethyl ether reduction of substrate (B12) which led to equal amounts of cis- and

trans-alkenols. However, the predominant product was the allene instead of the trans-alcohol. In the case of substrates (B13) and (B14), reactions with lithium aluminium hydride in diethyl ether gave allene as the sole product. Along the series (B11), (B12), (B13) and (B14), in diethyl ether, the overall near:far ratios were 86:8, 28:57, 0:90 and 0:99. The decreasing ratios of near:far were as before a reflection of the allene formation from 8 to 57 to 90 to 99 (%).

A comparative study of the epimeric substrates (B8) and (B11); (B9) and (B12); (B10) and (B13).

(a) The effect of the C1-configuration is shown (Tables 6 & 9) by the relative rates of reduction on β- and α-propynyl cyclic alcohols (B8) and (B11) respectively.

The comparative experiments on the reduction of the epimeric alcohols (B8) and (B11) showed that (B8) tends to give more allene than (B11). For example, the most notable difference in allene yield was seen in the diethyl ether reactions at 35^{o} for 96 h, from which 60% of allene was obtained for alkynol (B8) whereas the reduction of (B11) gave only 8% allene. There was also a great difference between the overall near:far ratios given by the two alcohols. Quite a wide range of near:far ratios were exhibited in the two tables. The lowest near:far value of 11:80 was obtained by reacting compound (B8) in 2,5-dimethyl-THF, and the highest near:far value of 86:8 was given by the reaction of compound (B11) in diethyl ether. Generally, higher near:far ratios characterized the reduction of the equatorial

alcohol (B11).

(b) It is interesting to note that, in contrast to the epimeric pair of compounds discussed above, no major differences in the overall near:far ratios were found for the reductions of the epimers (B9) and (B12) in the various ether solvents (Table 7 & 10). In the reduction of the epimeric alcohols (B9) and (B12) in diethyl ether or 2,5-dimethyl-THF a low near:far ratio was generally favoured, but when tetrahydrofuran was used near-carbon hydride attack was promoted and an almost unit near:far ratio was obtained. The extent of reduction displayed in Tables 7 & 10 showed that there was little difference in reactivity between the two isomers (B9) and (B12).

(c) Data presented in Tables 8 & 11 showed that with the exception of the reactions of tetrahydrofuran the reduction of the epimeric alcohols (B10) and (B13) gave low near:far ratios.

The differential effects of increased steric compression on the reactions on the axial and equatorial substrates can be clearly seen by comparing these two compounds with their unmethylated analogs (B8) and (B11). To better illustrate this point the reactions of four alcohols (B8), (B11), (B10) and (B13) in diethyl ether solvent will be discussed. For the axial alcohols (B8) and (B10), the near:far ratio changed from 22:71 to 11:76 on the introduction of methyls at C2 and C6, whereas a considerable change in the

near:far ratio was observed in the corresponding reductions of the equatorial alcohols (B11) and (B13), the ratio changing from 86:8 to 0:90.

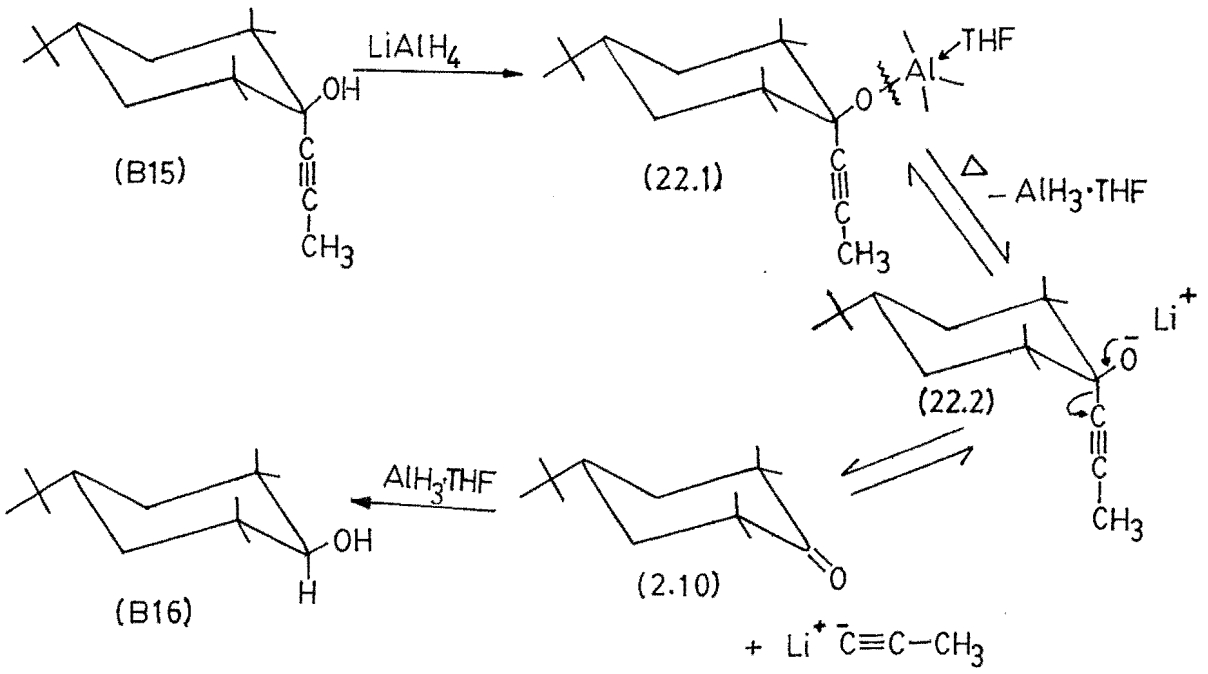
In the 2,5-dimethyl-THF reductionsof the epimeric alcohols (B10) and (B13), the near:far ratios were similar. In tetrahydrofuran, the axial alcohol (B10) gave high near: far ratio indicating more near-carbon attack, but there was a switch over to low near:far when the equatorial epimer (B13) was reduced under the same reaction conditions. Unfortunately, no such parallel study can be carried out on the trimethyl-alkynol (B14) as only one isomer was formed.

Reactions of 2,2,6,6-tetramethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ol (B15)

The presence of the four methyl groups at the 2 and 6 positions of the cyclohexyl propargyl alcohol (B15) would impose a severe steric strain on its reduction with lithium aluminium hydride. As expected, reactions of the alkynol (B15) have a tendency towards allene production and far-carbon hydride attack as revealed by the near:far ratios (Table 13). A notable exception was found in the tetra-hydrofuran reaction which gave a high proportion of 2,2,6,6-tetramethyl-4-α-t-butylcyclohexan-1-β-ol (B16). This secondary alcohol was also discovered as a side product in the first attempt to synthesize the alkynol (B15) by reacting 2,2,6,6-tetramethylcyclohexanone (2.10) with propynylmagnesium bromide, as discussed earlier. Reduction of the cylic ketone (2.10) with lithium aluminium hydride in diethyl ether gave the same compound (B16), with its

hydroxyl group equatorial.

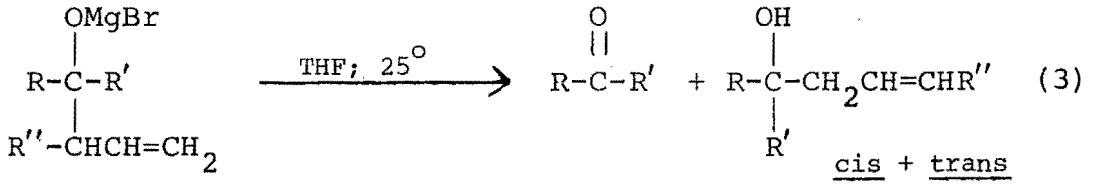
The formation of the secondary alcohol in the reduction of the sterically hindered alkynol (B15) was interesting because it would involve the postulation of a reversible mechanism outlined in Scheme 22. Presumably stabilization

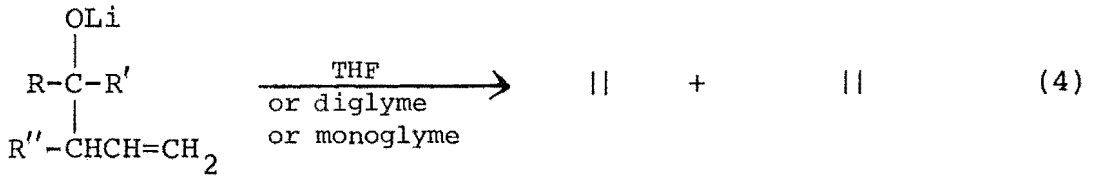


Scheme 22

of aluminium hydride (AlH_3) by THF[21] enabled cleavage of the oxygen-aluminium bond which led to the formation of the lithium alkoxide (22.2). Further degeneration of compound (22.2) gave the cyclic ketone (2.10), and the propynyllithium formed could also be stabilized in THF solvent due to the greater "incipient" solubility of the propynyllithium[53]. Reduction of the ketone (2.10) with aluminium hydride (AlH_3) afforded the secondary alcohol (B16).

The reverse reaction from ketone (2.10) to the lithium alkoxide (22.2) resembles the addition reaction of a Grignard or an organoalkyllithium reagent to a ketone. In the literature there is evidence of reversible addition of allylic-type Grignard and organolithium reagents to a variety of ketone substrate [52(a),(b)]. The effect of steric strain on the rate of reversal of a series of lithium and magnesium homoallylic alkoxides has been examined[52(b)] recently, equation (3) and (4). The alkoxides were prepared by the addition of n-butyllithium or





methylmagnesium bromide to the appropriate carbinol. Results showed that the rate of reversal increases as the steric bulk of the metal alkoxides increases; lithium alkoxides reversed about ten times faster than the corresponding magnesium bromoalkoxides.

APPENDIX

LANTHANIDE INDUCED SHIFT STUDIES

Introduction

The work discussed in Part II in this thesis required the synthesis of a number of substituted cyclohexylpropargyl alcohols, where two epimers may be formed. This necessitated the assignment of configuration at C_1 based on their n.m.r. chemical shifts of C_1 and the OH resonances, together with the use of Lanthanide Induced Shift (LIS) technique. In cases where only one epimer was formed a computational treatment of LIS data was employed to verify the uncertain stereochemistry.

Results

(1) Assignments of compounds. The specific assignment of carbons in the spectra are based on comparisons with model compounds, along with information obtained from the off-resonance spectra, see Tables 15 - 23, entry 1. It was shown[54] that introduction of an ethynyl group at C_1 in cyclohexanol does not result in any significant ^{13}C shift differences between the two compounds (see Table 14). On this basis two model compounds[55], cis- and trans-4-t-butylcyclohexanols, were used to assign the resonances of the cyclohexyl skeleton of alkynols (B8) and (B11) respectively (Tables 14, 15, 16). The C-1 resonance of alkynol (B11), with equatorial OH group, occurred at

lower field. This chemical shift disparity was also used as a basis for the assignments of the configuration at C_1 for the epimers (B9), (B12) and (B10), (B13). The assignments of resonances due to other carbons of (B8) and (B11) are unambiguous on account of their unique chemical shifts.

Upon introduction of a methyl group at C_2 in the cyclohexyl ring, C_3 was deshielded by about 8 ppm, see Tables 17 and 18. This compared well with the shift parameter (+9.0 ppm) given for the β methyl-substituent effect of cyclohexane system[56]. Surprisingly, the β effect at C_1 is only about +3.1 and +3.7 ppm for alkynols (B9) and (B12) respectively. The resonances due to other carbons did not shift much from those corresponding resonances of the unmethylated analogs and therefore could be readily assigned by comparisons. C_2 was deshielded in both (B9) and (B12) by about 1.8 ppm* and its assignment was confirmed by its appearance as a doublet in the (SFORD) spectrum.

Tables 19 and 20 show ~~that~~ the assignments for alkynols (B10) and (B13). As compared to the monomethylated compounds the replacement of a proton by a methyl group at C_6 further deshielded the C_1 atom by about 3.5 ppm*. In compound (B13), C_7 was assigned to the peak at 77.64 and the resonance at the lowest field, 82.91, was assigned to C_8. The reverse assignments, as compared to other assignments for alkyne carbons, are based on the greater

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* Average value.

Δ_1 value for C_7 obtained from the lanthanide shift experiments. The assignments for other carbons could be made unambiguously by comparisons with corresponding resonances in compounds (B9) and (B12).

In alkynol (B14), Table 21, the signal at 78.63 was assigned to C_1 on the basis of the large shift caused by adding $Yb(fod)_3$. The quaternary carbons, C_2 and C_{10}, appeared as a singlet in the (SFORD) spectrum and could be assigned without difficulty on account of their chemical shifts. By the same technique the methine carbons, C_4 and C_6, were assigned. For C_3 and C_5 which appeared as triplets (SFORD), the former was assigned to the resonance at the lower field (39.11) as it would be more deshielded by the two methyl groups at C_2[56]. C_5 was then assigned by default. The methyl carbons on the ring system may be assigned on the basis of their chemical shifts. C_{14}, being an equatorial substituent and attached to a quaternary carbon, was assigned to the lowest resonance of the three at 27.21. The resonance at 16.69 was assigned to C_{15} by comparison with C_{15} in compound (B13). C_{16} may then be assigned to 20.62 by default.

In compound (B15) the ring carbons ($C_{2,6}$; $C_{3,5}$; C_4) may be assigned unambiguously on the multiplicities of their resonances in the SFORD spectrum. C_1 resonance may again be distinguished from the resonances due to C_7 and C_8 by the large shift caused by adding $Yb(fod)_3$. C_7 and C_8 were assigned to the resonances at 82.61 and 81.68 respectively on account of the LIS bound shifts (Δ_1) obtained for C_7 and C_8. By the line intensity the resonance at 27.68 was assigned to the tert-butyl carbons. The remaining resonances

at 30.57 and 22.77 were assigned to $C_{14,15}$ and $C_{16,17}$ respectively on the basis that the equatorial methyl carbons would occur at lower field. As a comparison, in 2-methyl-norbornane the endo-methyl carbon is about 5 ppm upfield relative to the exo-methyl carbon[57]. The resonances in compound (B16) were assigned by applying the same techniques as above, and the chemical shifts are given in Table 23.

(2a) Lanthanide Induced Shift Data. The data for the LIS studies are given in Tables 15-26. The lanthanide induced n.m.r. shifts for the alcohols were determined by incremental addition of weighed amounts of the shift reagent [$Yb(fod)_3$ or $Eu(fod)_3$] to a solution of the alcohol (40 - 55 mg) in $CDCl_3$ (0.2 or 0.25 ml) and subsequent extrapolation of the observed chemical shifts (Δ) to a 1:1 molar ratio of shift reagent : alcohol gave the bound shifts (Δ_1).

A computational simulation of the LIS values was applied to substrates (B14), (B15) and (B16). The geometry of the substrate is described with respect to an internal Cartesian coordinate system (Figure 1). C_1 atom of the

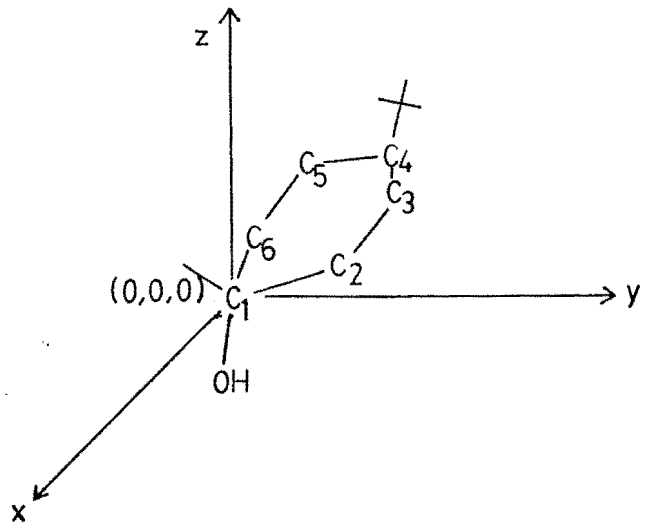


Fig.1

substrate is placed at the origin of the coordinate system, the xy plane is defined by the plane of atoms $C_1C_2C_6$, the line bisecting the angle $C_2\hat{C}_1C_6$ defines the negative x axis.

The chair conformation of the substrate (B14 or B15 or B16) was assumed initially and the geometry was derived by using the computer program XYZ[58] converting the standard internal coordinates (bond lengths, bond angles, dihedral angles) into Cartesian coordinates. With these coordinates a molecular mechanics calculation using program MMI[59] was applied, with standard parameters plus the addition of the following constants: V_1=0.27 for torsion round the C_1-O bond and K_θ=0.560 for C_{sp}-C_1-O bond-bending. A new set of coordinates was obtained corresponding to a refined geometry with the least strain energy.

The shift for each position atom was calculated using McConnell-Robertson equation (1)[60]; r_i is the

$$\Delta_i^{calc} = K \cdot (3\cos^2\theta_i - 1)/r_i^3 \qquad (1)$$

distance between the lanthanide ion and the i^{th} atom, and θ_i is the angle made by the vector corresponding to r_i and the principal magnetic axis of the complex (normally taken to be represented by the vector lanthanide ion-coordination center). K is assumed to be a constant for a given lanthanide and temperature, and is treated as an adjustable scaling factor to match the observed LIS values to the geometrical factor $(3\cos^2\theta_i - 1)/r_i^3$. After scaling, the calculated and observed LIS values were compared using the statistical R factor (equation 2). The weighting factors

$$R = \left[\frac{\sum_i (\Delta_i^{obs} - \Delta_i^{calc})^2 \omega_i}{\sum_i (\Delta_i^{obs})^2 \omega_i} \right]^{\frac{1}{2}} \qquad (2)$$

(ω_i) are introduced; ω_i=1 for every non-equivalent nucleus yielding a LIS value and ω_i=1/n (n $\geqslant$ 2) for a group of n equivalent nuclei giving the same resonance signal in the n.m.r. spectrum. The C_1 and hydroxyl proton resonances were excluded in the above calculation due to contact shift-contribution[61]. The coordinates of the lanthanide ion and the McConnell-Robertson K factor were optimised with respect to the R factor using the VA04A subroutine[68].

The above procedures were repeated by assuming a new substrate topology corresponding to the other epimeric counterpart, and again the final best R factor was obtained for an optimal arrangement of the lanthanide ion. To decide between the two isomers the geometry R factor, (R_1) can be tested against the other (R_2) by taking the ratio R_1/R_2 (for $R_1 > R_2$). This significance testing using Hamilton's tables[62] was shown to be inappropriate to n.m.r. applications[63], which involve only a small number of degrees of freedom. However, the ratios obtained (Tables 24-26) were sufficiently large that R_1 geometry can be rejected unquestionably in favour of the R_2 geometry.

(2b) Results and Discussion. The bound chemical shifts (Δ_1) for alkynols (B8-13) are given in Tables 15-20. Assuming the angular term in the McConnell-Robertson

equation (1) as constant and taking r as the distance from the coordination center (in this case the oxygen atom) to the nucleus, simple correlations of Δ_1 values with one substrate geometry can be compared with those of another geometry. In the axial alcohols (B8-10) the ratios of $\Delta_1(C_2/C_3)$ or (C_6/C_5) range from 1 - 1.5, and as expected a larger range was obtained for the equatorial alcohols (B11-13), 2 - 2.5. By this simple distance relationship it may be sufficient to verify the configurational assignments made on the basis of n.m.r. data for OH and C_1 resonances as well as the difference in polarity between the axial and equatorial alcohols.

The observed and calculated bound shifts (Δ_1) for substrates (B14-16) are given in Tables 24-26 along with their R factors and the R_1/R_2 ratio between two configurational isomers. The one-site model employed is one in which the calculated LIS shifts were obtained when the lanthanide-substrate was in the optimal arrangement, and for the two-site model the calculated shifts were averaged between two best lanthanide positions which were mirror images with respect to the plane perpendicular to that made by the C_2-C_1-C_6 bonds.

The results show that in every case the geometry bearing the equatorial hydroxyl group was preferred over the axial-OH geometry. The R_1/R_2 ratio (8.97) for compound (B16) is extremely high thus the equatorial-OH geometry can be accepted with a high level of confidence. Interestingly, for compounds (B15) and (B16) it is noted that the favoured geometries have a higher strain energy as a consequence of the relative high energy due to angle bending, 14.32 and

13.14 Kcal respectively. The 2-site model suggested[67] gave poorer agreement with experiment than a 1-site model for compound (B14), and for compound (B16) there is no difference at all. Better results were obtained by using the MMI coordinates than the standard coordinates as shown in Table 25.

Table 27 shows the geometries of 4-t-butylcyclohexanone, 4-t-butyl-1-methylene cyclohexane and the three alkynols (B14), (B15), (B16). The geometry of 4-t-butylcyclohexanone was determined by X-ray diffraction and NMR coupling constants, which compares reasonably well with the MMI geometry of 4-t-butyl-1-methylene cyclohexane. The internal angles $C_3\hat{C}_4C_5$ of all the compounds do not differ much from one another, as expected, since the structure at this end of the molecule is similar in each case. In contrast, the $C_6\hat{C}_1C_2$ angle (119.9) of substrate (B16) is prominently larger than that of others and therefore the least buckled at the hydroxyl end of the molecule. This ring flattening is also shown by the small values of the dihedral angles ω_{12} and ω_{16} as compared to compounds (B14) and (B15). Compound (B15) is flatter than (B14) at the C_1 end of the molecule as evident by the relatively larger $C_6\hat{C}_1C_2$ and smaller dihedral angles ω_{12} and ω_{16}.

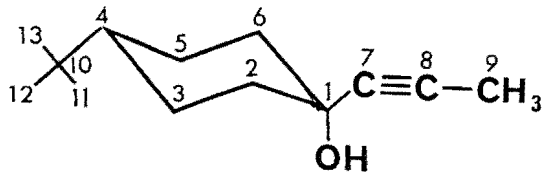
The final parameters for bond lengths and bond angles of compounds (B14), (B15) and (B16), as extracted from MMI calculations, are listed in Tables 28-33. The stereoscopic views of the molecular structure of compound (B15) are given in Diagrams 1, 2 and 3.

TABLE 14

^{13}C N.m.r. SHIFTS (ppm) FOR ALKYNOLS (B8, B11), AND RELATED COMPOUNDS

Compound	C_1	C_2	C_3	C_4	C_5	C_6
Cyclohexanol	69.8	35.8	24.7	26.2	24.7	35.8
1-Ethynylcyclohexanol	68.6	39.7	25.1	25.1	25.1	39.7
cis-4-t-Butylcyclohexanol	65.0	33.3	21.0	48.2	21.0	33.3
Alkynol (B8)	65.9	39.8	22.1	47.5	22.1	39.8
trans-4-t-Butylcyclohexanol	70.4	35.7	25.7	47.3	25.7	35.7
Alkynol (B11)	69.7	40.7	25.0	47.3	25.0	40.7

TABLE 15. OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALKYNOL (B8) - Yb(fod)$_3$ [a]

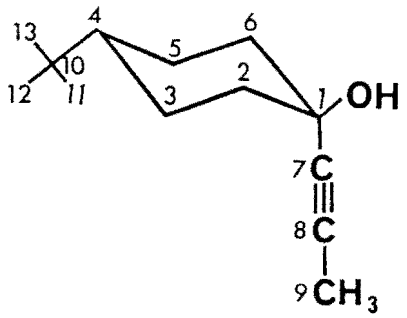


ρ(x10^{-1}) [b]	C_1	$C_{2,6}$	$C_{3,5}$	C_4	C_7	C_8	C_9	C_{10}	$C_{11,12,13}$
0.00	65.91	39.79	22.07	47.45	85.14	77.82	3.47	32.46	27.58
0.55	67.28	40.42	22.46	47.75	86.07	78.26	3.51	32.61	27.65
0.97	68.31	40.91	22.80	48.00	86.76	78.66	3.61	32.75	27.76
1.43	69.33	41.40	23.09	48.23	87.47	79.00	3.66	32.84	27.82
1.79	70.20	41.79	23.35	48.39	88.03	79.29	3.71	32.90	27.87
Δ_1	24.1	11.2	7.3	5.5	16.2	8.3	1.4	2.8	1.8
$\Delta_1(C_2/C_3),(C_6/C_5)$		1.53							

[a] $[S_o]$ = 1.0292M

[b] $\rho = [L]/[S_o]$

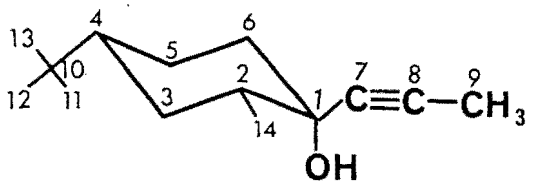
TABLE 16 OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALKYNOL (B11)-Yb(fod)$_3$ [a]



ρ(x10^{-1}) [b]	C_1	$C_{2,6}$	$C_{3,5}$	C_4	C_7	C_8	C_9	C_{10}	$C_{11,12,13}$
0.00	69.72	40.71	24.98	47.26	82.60	80.59	3.50	32.27	27.68
0.44	70.83	41.27	25.23	47.45	83.20	80.92	3.60	32.36	27.73
0.82	71.98	41.85	25.48	47.61	83.79	81.25	3.72	32.42	27.79
1.30	73.01	42.38	25.69	47.80	84.32	81.54	3.81	32.52	27.84
1.94	74.80	43.31	26.12	48.09	85.25	82.08	4.00	32.66	27.97
Δ_1	26.1	13.3	5.8	4.2	13.8	7.6	2.6	2.0	1.3
$\Delta_1(C_2/C_3),(C_6/C_5)$		2.29							

[a] $[S_o]$ = 1.0292M [b] $\rho = [L]/[S_o]$

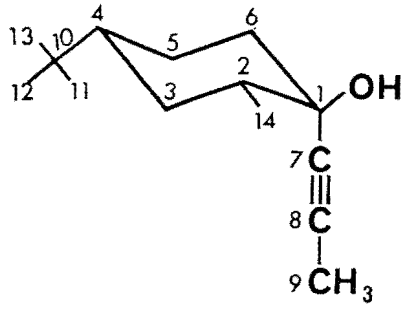
TABLE 17 OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALKYNOL (B9)-Eu(fod)$_3$ [a]



ρ(x10^{-1}) [b]	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	$C_{11,12,13}$	C_{14}
0.00	69.03	41.35	30.22	47.70	21.77	40.67	84.08	78.66	3.50	32.37	27.53	16.69
1.08	70.70	41.65	30.53	47.90	22.07	41.16	85.15	79.19	3.57	32.47	27.59	17.04
1.35	71.42	41.77	30.69	48.02	22.20	41.35	85.64	79.46	3.64	32.49	27.62	17.19
2.66	73.67	42.18	31.10	48.29	22.60	41.98	87.15	80.16	3.75	32.60	27.68	17.66
3.20	74.61	42.33	31.26	48.39	22.75	42.24	87.75	80.46	3.81	32.66	27.71	17.83
Δ_1	17.5	3.1	3.2	2.0	3.1	4.8	11.4	5.6	0.9	0.9	0.6	3.6
$\Delta_1(C_2/C_3),(C_6/C_5)$			0.97			1.55						

[a] $[S_o]$ = 1.2959M [b] $\rho = [L]/[S_o]$

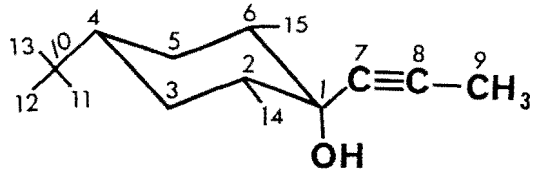
TABLE 18 OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALKYNOL (B12)-Eu(fod)$_3$ [a]



ρ(x10^{-1}) [b]	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	$C_{11,12,13}$	C_{14}
0.00	73.44	42.72	33.44	47.47	25.20	41.31	81.95	79.98	3.47	32.23	27.64	16.36
0.44	74.03	42.92	33.55	47.56	25.30	41.56	82.08	80.08	3.52	32.23	27.65	16.51
1.17	75.38	43.44	33.77	47.74	25.57	42.17	82.40	80.37	3.67	32.30	27.72	16.88
1.89	76.74	43.92	34.01	47.89	25.81	42.80	82.69	80.60	3.79	32.41	27.76	17.23
3.01	78.80	44.67	34.34	48.15	26.18	43.74	83.21	81.04	4.01	32.53	27.88	17.78
3.98	80.71	45.38	34.69	48.37	26.54	44.62	83.65	81.47	4.22	32.64	27.96	18.29
Δ_1	16.9	6.5	3.0	2.2	3.2	8.1	4.0	3.5	1.7	1.0	0.8	4.8
$\Delta_1(C_2/C_3)$,(C_6/C_5)		2.17				2.53						

[a] $[S_o]$ = 1.0319M [b] $\rho = [L]/[S_o]$

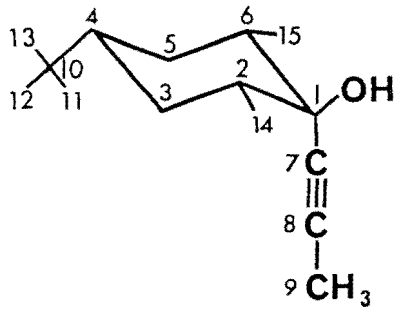
TABLE 19 OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALKYNOL (B10)-Yb(fod)$_3$ [a]



ρ(x10^{-1}) [b]	C_1	$C_{2,6}$	$C_{3,5}$	C_4	C_7	C_8	C_9	C_{10}	$C_{11,12,13}$	$C_{14,15}$
0.00	72.30	42.21	30.02	47.14	83.09	79.47	3.42	32.26	27.53	16.88
0.61	72.71	42.43	30.23	47.27	83.40	79.68	3.52	32.32	27.59	17.07
0.98	72.94	42.57	30.31	47.36	83.59	79.80	3.50	32.36	27.62	17.18
1.45	73.33	42.81	30.51	47.51	83.85	80.03	3.61	32.49	27.70	17.35
2.06	73.87	43.10	30.78	47.70	84.27	80.31	3.74	32.60	27.79	17.61
Δ_1	7.3	4.1	3.5	2.5	5.5	3.8	1.4	1.4	1.2	3.3
$\Delta_1(C_2/C_3),(C_6/C_5)$		1.17								

[a] $[S_o] = 0.9893M$ [b] $\rho = [L]/[S_o]$

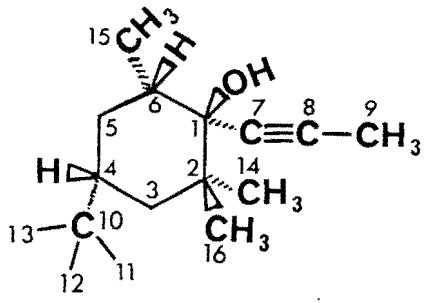
TABLE 20 OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALKYNOL (B13)-Yb(fod)$_3$ [a]



ρ(x10^{-1}) [b]	C_1	$C_{2,6}$	$C_{3,5}$	C_4	C_7	C_8	C_9	C_{10}	$C_{11,12,13}$	$C_{14,15}$
0.00	77.24	43.11	33.69	46.98	77.64	82.91	3.37	32.13	27.59	16.31
0.50	78.57	43.84	34.02	47.24	78.31	83.34	3.56	32.27	27.69	16.79
0.80	79.68	44.42	34.27	47.41	78.80	83.69	3.69	32.32	27.74	17.14
1.51	81.41	45.35	34.71	47.75	79.68	84.27	3.94	32.51	27.87	17.76
2.24	82.96	46.19	35.09	48.04	80.42	84.80	4.14	32.66	27.97	18.30
Δ_1	27.9	14.7	6.6	5.0	13.3	9.1	3.6	2.4	1.7	9.5
$\Delta_1(C_2/C_3),(C_6/C_5)$		2.23								

[a] $[S_o]$ = 0.9893M [b] $\rho = [L]/[S_o]$

TABLE 21. OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALKYNOL (B14)-Yb(fod)$_3$ [a]



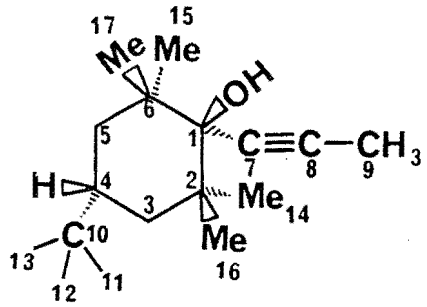
ρ(x10^{-1}) [b]	C_1	C_2	C_3	C_4	C_5	C_6	C_7 **	C_8 **	C_9	C_{10}	$C_{11,12,13}$	C_{14}	C_{15}	C_{16}	H_3-9	H_3-14	H_3-15	H_3-16	H_3-11,12,13
0.00	78.63	38.98	39.11	41.86	33.70	36.83	82.54	79.25	3.33	31.90	27.46	27.21	16.69	20.62	2.48	1.45	1.35	1.30	1.11
0.57	79.20	39.22	39.22	41.95	33.84	37.24	-	-	3.37	31.80*	27.49	27.41	16.88	20.84	2.55	1.68	1.58	1.56	1.18
1.16	79.88*	39.65*	39.54	42.23	34.13	37.64*	-	-	3.55	32.50*	27.68	27.68	17.23	21.23	2.71	2.00	1.90	1.94	1.28
2.75	81.13	40.36	39.88	42.51	34.50	38.37	-	-	3.74	32.25	27.77	28.20	17.74	21.76	2.91	2.53	2.45	2.56	1.40
3.25	81.69	40.66	40.04	42.62	34.66	38.71	-	-	3.80	32.32	27.82	28.41	17.96	22.01	2.99	2.76	2.71	2.85	1.45
3.80	82.23	40.92	40.18	42.73	34.79	39.02	-	-	3.86	32.37	27.85	28.61	18.16	22.23	3.06	2.99	2.90	3.13	1.51
Δ_1	9.4	5.1	2.9	2.3	2.9	5.8	-	-	1.5	1.3	1.1	3.7	3.9	4.2	1.6	4.1	4.1	4.9	1.1

[a] $[S_o]$ = 1.1430M

[b] $\rho = [L]/[S_o]$.

* Value not included in the plot of Δ vs. ρ. ** Signals not observed after adding Yb(fod)$_3$ reagent.

TABLE 22. OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) FOR ALKYNOL (B15)-Yb(fod)$_3$ [a]

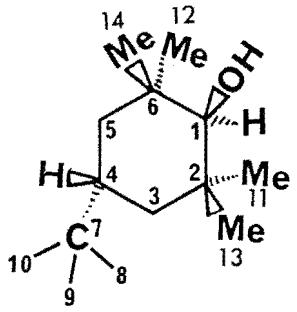


ρ(x10^{-1})[b]	C_1	$C_{2,6}$	$C_{3,5}$	C_4	C_7	C_8	C_9	C_{10}	$C_{11,12,13}$	$C_{14,15}$	$C_{16,17}$	H_3-14,15	H_3-16,17	H_4	H_3-9	H_3-11,12,13
0.00	79.19	39.65	39.26	38.92	82.61	81.68	3.32	31.78	27.68	30.57	22.77	1.81	1.69	2.16	2.93	1.36
1.51	80.06	40.14	39.55	39.11	-	82.12	3.47	31.93	27.78	30.96	23.14	2.29	2.18	2.45	3.08	1.48
3.09	81.05	40.67	39.84	39.40	83.92	82.66	3.67	32.08	27.89	31.39	23.58	2.88	2.79	2.85	3.28	1.63
4.87	82.09	41.22	40.15	39.61	84.63	83.16	3.82	32.18	27.99	31.79	23.98	3.46	3.38	3.18	3.48	1.78
6.51	83.10	41.74	40.43	39.84	85.34	83.69	3.96	32.31	28.08	32.18	24.41	4.00	3.95	3.58	3.63	1.93
Δ_1	5.86	3.21	1.82	1.42	4.07	3.60	1.40	0.88	0.65	2.51	2.51	2.11	2.17	1.35	0.70	0.53

[a] $[S_o]$ = 1.0981M

[b] $\rho = [L]/[S_o]$

TABLE 23. OBSERVED SHIFTS (δ) (ppm) AND BOUND SHIFTS (Δ_1) (ppm) FOR ALCOHOL (B16) - Yb(fod)$_3$[a]



$\rho(x10^{-1})$[b]	C_1	$C_{2,6}$	C_4	$C_{3,5}$	C_7	$C_{8,9,10}$	$C_{11,12}$	$C_{13,14}$	H_1	H_3-11,12	H_3-13,14	H_3-8,9,10
0.00	84.34	36.18	38.91	41.35	31.73	27.58	32.50	20.16	2.93	0.97	0.90	0.84
0.44	85.98	36.91	39.20	41.69	31.82	27.67	32.93	20.69	3.96	1.37	1.29	0.94
1.25	88.78	38.29	39.74	42.34	32.18	27.93	33.75	21.72	4.76	2.15	1.81	1.10
1.89	90.81	39.26	40.12	42.77	32.32	28.06	34.32	22.41	7.00	2.74	2.20	1.21
2.82	94.38	40.96	40.72	43.51	32.61	28.27	35.30	23.63	9.30	3.79	2.93	1.43
3.21	95.55	41.51	40.92	43.75	32.71	28.34	35.62	24.02	10.00	4.11	3.14	1.48
Δ_1	35.5	16.8	6.6	7.9	3.5	2.6	10.1	12.5	21.6	9.6	6.9	1.9

[a] $[S_o] = 1.2723M$ [b] $\rho = [L]/[S_o]$

TABLE 24

EXPERIMENTAL AND CALCULATED BOUND SHIFTS (Hz) FOR ALKYNOL (B14) ALONG WITH THE FINAL PARAMETERS FOR THE STRAIN ENERGY (Kcal).

	Experimental	1-site model Calculated		2-site model Calcualted	
		Eq.OH	Ax.OH	Eq.OH	Ax.OH
C_2	411.2	414.6	391.8	437.1	450.8
C_3	232.0	220.2	312.8	226.9	304.2
C_4	180.0	176.6	219.1	271.1	211.6
C_5	232.0	219.6	302.9	220.0	305.4
C_6	464.0	428.1	444.1	411.0	427.4
C_9	120.0	141.8	106.1	128.2	95.5
C_{10}	104.0	103.1	106.1	88.6	88.0
$C_{11,12,13}$	88.0	81.4	67.0	63.3	46.8
C_{14}	296.0	330.3	335.6	361.6	378.9
C_{15}	338.4	364.4	363.9	373.9	328.9
C_{16}	312.0	369.3	212.7	329.4	210.7
H_3-9	125.0	115.7	73.9	122.9	64.8
H_3-14	330.0	298.1	331.7	325.8	333.4
H_3-15	330.0	340.7	323.0	349.8	281.6
H_3-16	389.0	342.0	174.6	293.8	164.9
R(%)		9.32	24.96	12.97	27.29
R ratio		2.69		2.10	
Bond-stretch		3.51	3.48		
Angle-bend		6.31	6.29		
Stretch-bend		0.61	0.60		
Non-bonded		7.58	7.79		
Torsional		0.59	0.70		
Torsion-bend		-0.02	-0.02		
Strain energy		18.87	19.30		

TABLE 25

EXPERIMENTAL AND CALCULATED BOUND SHIFTS (Hz) FOR ALKYNOL (B15) ALONG WITH THE FINAL PARAMETERS FOR THE STRAIN ENERGY (Kcal).

		2-site model			
		Standard Coordinates		MMI Coordinates	
	Experimental	Eq.OH	Ax.OH	Eq.OH	Ax.OH
$C_{2,6}$	266.8	321.8	300.5	220.2	198.7
$C_{3,5}$	145.6	148.6	213.6	131.1	144.6
C_4	113.6	114.7	143.1	105.8	114.3
C_7	325.6	312.9	302.3	339.7	339.4
C_8	288.0	173.0	151.1	291.3	288.1
C_9	112.0	84.3	59.2	112.5	114.3
C_{10}	70.4	63.3	43.3	64.8	78.9
$C_{11,12,13}$	52.0	49.3	6.4	51.7	66.7
$C_{14,15}$	200.8	227.6	213.8	218.0	223.2
$C_{16,17}$	200.8	207.3	144.8	180.8	126.5
H_3-9	55.6	69.9	42.9	53.6	58.8
H_3-14,15	173.8	158.7	118.0	211.9	229.6
H_3-16,17	168.8	186.8	177.9	167.6	107.6
H_3-11,12,13	42.5	45.0	-6.1	47.6	62.8
H_2-3,5	108.1	114.4	187.0	110.4	134.6
H-4	108.1	90.8	104.3	99.4	95.9
R(%)		19.76	30.95	10.16	20.15
R ratio		1.566		1.983	
Bond-stretch				4.56	4.42
Angle-bend				14.32	9.10
Stretch-bend				0.63	0.69
Non-bonded				9.24	8.72
Torsional				1.56	1.28
Torsion-bend				-0.03	-0.05
Strain energy				30.96	24.74

TABLE 26

EXPERIMENTAL AND CALCULATED BOUND SHIFTS (Hz) FOR ALKYNOL (B16) ALONG WITH THE FINAL PARAMETERS FOR THE STRAIN ENERGY (Kcal).

		1-site model Calculated		2-site model Calculated	
	Experimental	Eq.OH	Ax.OH	Eq.OH	Ax.OH
$C_{2,6}$	1344	1357.3	1437.1	1357.4	1439.9
$C_{3,5}$	630	632.5	818.7	632.3	815.2
C_4	528	513.1	568.2	513.0	565.4
$C_{11,12}$	808	814.0	921.4	814.0	922.0
$C_{13,14}$	1000	960.8	630.3	960.8	630.1
C_7	280	272.0	204.4	271.9	202.4
$C_{8,9,10}$	208	204.5	101.4	204.5	100.0
H_3-11,12	550	545.1	478.1	545.2	530.1
H_3-13,14	770	795.5	528.7	795.5	477.4
H_3-8,9,10	150	182.7	66.4	182.6	65.3
R(%)		2.71	24.29	2.71	24.30
R ratio		8.96		8.97	
Bond-stretch		4.02	4.03		
Angle-bend		13.14	8.11		
Stretch-bend		0.76	0.78		
Non-bonded		9.09	8.92		
Torsional		1.26	1.27		
Torsion-bend		-0.07	-0.07		
Strain energy		28.21	23.04		

TABLE 27

COMPARATIVE GEOMETRIES OF ALKYNOLS (B14), (B15), (B16) AND RELATED COMPOUNDS

Compound	Bond Angles [a]				Torsional Angles [b]						Technique and Reference
	C_1	C_2	C_3	C_4	ω_{12}	ω_{23}	ω_{34}	ω_{45}	ω_{56}	ω_{16}	
B14	112.9	108.5	116.8	108.7	-52.9	53.2	-52.3	51.4	-54.6	55.1	MMI, this work
B15	116.7	107.8	116.1	109.3	-52.6	53.1	-52.5	50.5	-49.6	51.1	MMI, this work
B16	119.9	107.6	115.9	108.8	-48.2	51.5	-55.0	53.0	-48.1	46.8	MMI, this work
4-t-Butylcyclohexanone	115.5	112.1	112.5	109.0	-47.4	52.1	-56.6				X-ray,[64,65]
						53.6	-56.6				NMR[66]
4-t-Butyl-1-methylene cyclohexane	115.0	110.1	112.0	109.6	-52	53.8	-56.7				MM,[67]

[a] The internal angle, i.e. C_1 is $C_6\hat{C}_1C_2$, etc.

[b] The C.C.C.C. angle, i.e. ω_{12} is for $C_6C_1C_2C_3$, etc.

Compound (B14)

TABLE 28 - BOND LENGTHS

C(1) - C(2)	1.54	C(12) - H(36)	1.10
C(1) - C(6)	1.54	C(12) - H(37)	1.09
C(1) - C(7)	1.48	C(12) - H(38)	1.10
C(1) - O(18)	1.39	C(13) - H(39)	1.10
C(2) - C(3)	1.54	C(13) - H(40)	1.09
C(2) - C(14)	1.55	C(13) - H(41)	1.10
C(2) - C(16)	1.54	C(14) - H(23)	1.10
C(3) - C(4)	1.54	C(14) - H(24)	1.10
C(3) - H(42)	1.10	C(14) - H(25)	1.10
C(3) - H(43)	1.09	C(15) - H(29)	1.10
C(4) - C(5)	1.54	C(15) - H(30)	1.10
C(4) - C(10)	1.56	C(15) - H(31)	1.10
C(4) - H(46)	1.10	C(16) - H(26)	1.10
C(5) - C(6)	1.53	C(16) - H(27)	1.09
C(5) - H(44)	1.10	C(16) - H(28)	1.10
C(5) - H(45)	1.10	O(18) - H(19)	0.94
C(6) - C(15)	1.54	O(18) - LP(32)	0.50
C(6) - H(17)	1.10		
C(7) - C(8)	1.21		
C(8) - C(9)	1.47		
C(9) - H(20)	1.10		
C(9) - H(21)	1.10		
C(9) - H(22)	1.10		
C(10) - C(11)	1.54		
C(10) - C(12)	1.55		
C(10) - C(13)	1.55		
C(11) - H(33)	1.10		
C(11) - H(34)	1.09		
C(11) - H(35)	1.09		

Compound (B14)

TABLE 29 - BOND ANGLES

C(2) - C(1) - C(6)	112.9	C(1) - O(18) - LP(32)	104.3
C(2) - C(1) - C(7)	110.6	H(19) - O(18) - LP(32)	100.4
C(2) - C(1) - O(18)	110.8		
C(6) - C(1) - C(7)	107.7		
C(6) - C(1) - O(18)	108.6		
C(7) - C(1) - O(18)	106.0		
C(1) - C(2) - C(3)	108.5		
C(1) - C(2) - C(14)	109.3		
C(1) - C(2) - C(16)	112.0		
C(3) - C(2) - C(14)	109.3		
C(3) - C(2) - C(16)	111.3		
C(14) - C(2) - C(16)	106.5		
C(2) - C(3) - C(4)	116.8		
C(3) - C(4) - C(5)	108.7		
C(3) - C(4) - C(10)	115.7		
C(5) - C(4) - C(10)	115.5		
C(4) - C(5) - C(6)	113.9		
C(1) - C(6) - C(5)	111.3		
C(1) - C(6) - C(15)	111.4		
C(5) - C(6) - C(15)	112.3		
C(1) - C(7) - C(8)	178.8		
C(7) - C(8) - C(9)	179.6		
C(4) - C(10) - C(11)	112.9		
C(4) - C(10) - C(12)	110.7		
C(4) - C(10) - C(13)	110.7		
C(11) - C(10) - C(12)	107.8		
C(11) - C(10) - C(13)	107.8		
C(12) - C(10) - C(13)	106.7		
C(1) - O(18) - H(19)	110.9		

Compound (B15)

TABLE 30 - BOND LENGHTS

C(1) - C(2)	1.55	C(12) - H(38)	1.10
C(1) - C(6)	1.55	C(12) - H(39)	1.09
C(1) - C(7)	1.48	C(12) - H(40)	1.10
C(1) - O(18)	1.38	C(13) - H(41)	1.10
C(2) - C(3)	1.54	C(13) - H(42)	1.09
C(2) - C(14)	1.55	C(13) - H(43)	1.10
C(2) - C(16)	1.54	C(14) - H(23)	1.10
C(3) - C(4)	1.54	C(14) - H(24)	1.10
C(3) - H(44)	1.10	C(14) - H(25)	1.10
C(3) - H(45)	1.09	C(16) - H(26)	1.09
C(4) - C(5)	1.54	C(16) - H(27)	1.09
C(4) - C(10)	1.56	C(16) - H(28)	1.10
C(4) - H(48)	1.10	C(15) - H(29)	1.10
C(5) - C(6)	1.54	C(15) - H(30)	1.09
C(5) - H(46)	1.10	C(15) - H(31)	1.10
C(5) - H(47)	1.09	C(17) - H(32)	1.10
C(6) - C(15)	1.55	C(17) - H(33)	1.09
C(6) - C(17)	1.54	C(17) - H(34)	1.10
C(7) - C(8)	1.21	O(18) - H(19)	0.93
C(8) - C(9)	1.47	O(18) - LP(49)	0.50
C(9) - H(20)	1.10		
C(9) - H(21)	1.10		
C(9) - H(22)	1.10		
C(10) - C(11)	1.54		
C(10) - C(12)	1.55		
C(10) - C(13)	1.55		
C(11) - H(35)	1.10		
C(11) - H(36)	1.09		
C(11) - H(37)	1.09		

Compound (B15)

TABLE 31 - BOND ANGLES

C(2) - C(1) - C(6)	116.7	C(11) - C(10) - C(13)	107.8
C(2) - C(1) - C(7)	107.1	C(12) - C(10) - C(13)	106.6
C(2) - C(1) - O(18)	110.6	C(1) - O(18) - LP(49)	116.4
C(6) - C(1) - C(7)	107.8	C(1) - O(18) - H(19)	125.1
C(6) - C(1) - O(18)	108.2	H(19) - O(18) - LP(49)	118.5
C(7) - C(1) - O(18)	105.9		
C(1) - C(2) - C(3)	107.8		
C(1) - C(2) - C(14)	108.4		
C(1) - C(2) - C(16)	115.5		
C(3) - C(2) - C(14)	109.6		
C(3) - C(2) - C(16)	110.6		
C(14) - C(2) - C(16)	104.8		
C(2) - C(3) - C(4)	116.1		
C(3) - C(4) - C(5)	109.3		
C(3) - C(4) - C(10)	115.5		
C(5) - C(4) - C(10)	115.7		
C(4) - C(5) - C(6)	116.6		
C(1) - C(6) - C(5)	108.9		
C(1) - C(6) - C(15)	108.6		
C(1) - C(6) - C(17)	112.9		
C(5) - C(6) - C(15)	109.4		
C(5) - C(6) - C(17)	111.7		
C(16) - C(6) - C(17)	105.2		
C(1) - C(7) - C(8)	179.1		
C(7) - C(8) - C(9)	179.6		
C(4) - C(10) - C(11)	113.0		
C(4) - C(10) - C(12)	110.8		
C(4) - C(10) - C(13)	110.7		
C(11) - C(10) - C(12)	107.7		

Compound (B16)

TABLE 32 - BOND LENGTHS

C(1) - C(2)	1.54	C(10) - H(39)	1.10
C(1) - C(6)	1.54	C(11) - H(19)	1.10
C(1) - H(45)	1.10	C(11) - H(20)	1.10
C(1) - O(16)	1.39	C(11) - H(21)	1.10
C(2) - C(3)	1.54	C(13) - H(22)	1.09
C(2) - C(11)	1.55	C(13) - H(23)	1.09
C(2) - C(13)	1.54	C(13) - H(24)	1.10
C(3) - C(4)	1.54	C(12) - H(25)	1.10
C(3) - H(40)	1.09	C(12) - H(26)	1.10
C(3) - H(41)	1.10	C(12) - H(27)	1.10
C(4) - C(5)	1.54	C(14) - H(28)	1.10
C(4) - C(7)	1.58	C(14) - H(29)	1.09
C(4) - H(44)	1.10	C(14) - H(30)	1.10
C(5) - C(6)	1.54	O(16) - H(17)	0.93
C(5) - H(42)	1.10	O(16) - LP(18)	0.50
C(5) - H(43)	1.10		
C(6) - C(12)	1.55		
C(6) - C(14)	1.54		
C(7) - C(8)	1.54		
C(7) - C(9)	1.55		
C(7) - C(10)	1.55		
C(8) - H(31)	1.10		
C(8) - H(32)	1.09		
C(8) - H(33)	1.09		
C(9) - H(34)	1.10		
C(9) - H(35)	1.09		
C(9) - H(36)	1.10		
C(10) - H(37)	1.10		
C(10) - H(38)	1.09		

Compound (B16)

TABLE 33 - BOND ANGLES

C(2)	- C(1)	- C(6)	119.9	C(9)	- C(7)	- C(10)	106.5
C(2)	- C(1)	- H(45)	105.1	C(1)	- O(16)	- H(17)	123.4
C(2)	- C(1)	- O(16)	112.2	C(1)	- O(16)	- LP(18)	118.6
C(6)	- C(1)	- H(45)	106.1	H(17)	- O(16)	- LP(18)	117.9
C(6)	- C(1)	- O(16)	109.4				
H(45)	- C(1)	- O(16)	102.4				
C(1)	- C(2)	- C(3)	107.6				
C(1)	- C(2)	- C(11)	108.5				
C(1)	- C(2)	- C(13)	114.3				
C(3)	- C(2)	- C(11)	109.4				
C(3)	- C(2)	- C(13)	111.0				
C(11)	- C(2)	- C(13)	105.9				
C(2)	- C(3)	- C(4)	115.9				
C(3)	- C(4)	- C(5)	108.8				
C(3)	- C(4)	- C(7)	115.8				
C(5)	- C(4)	- C(7)	115.6				
C(4)	- C(5)	- C(6)	116.4				
C(1)	- C(6)	- C(5)	108.8				
C(1)	- C(6)	- C(12)	108.5				
C(1)	- C(6)	- C(14)	111.9				
C(5)	- C(6)	- C(12)	109.4				
C(5)	- C(6)	- C(14)	112.1				
C(12)	- C(6)	- C(14)	106.1				
C(4)	- C(7)	- C(8)	112.7				
C(4)	- C(7)	- C(9)	110.9				
C(4)	- C(7)	- C(10)	110.8				
C(8)	- C(7)	- C(9)	107.8				
C(18)	- C(7)	- C(10)	107.8				

DIAGRAM 1

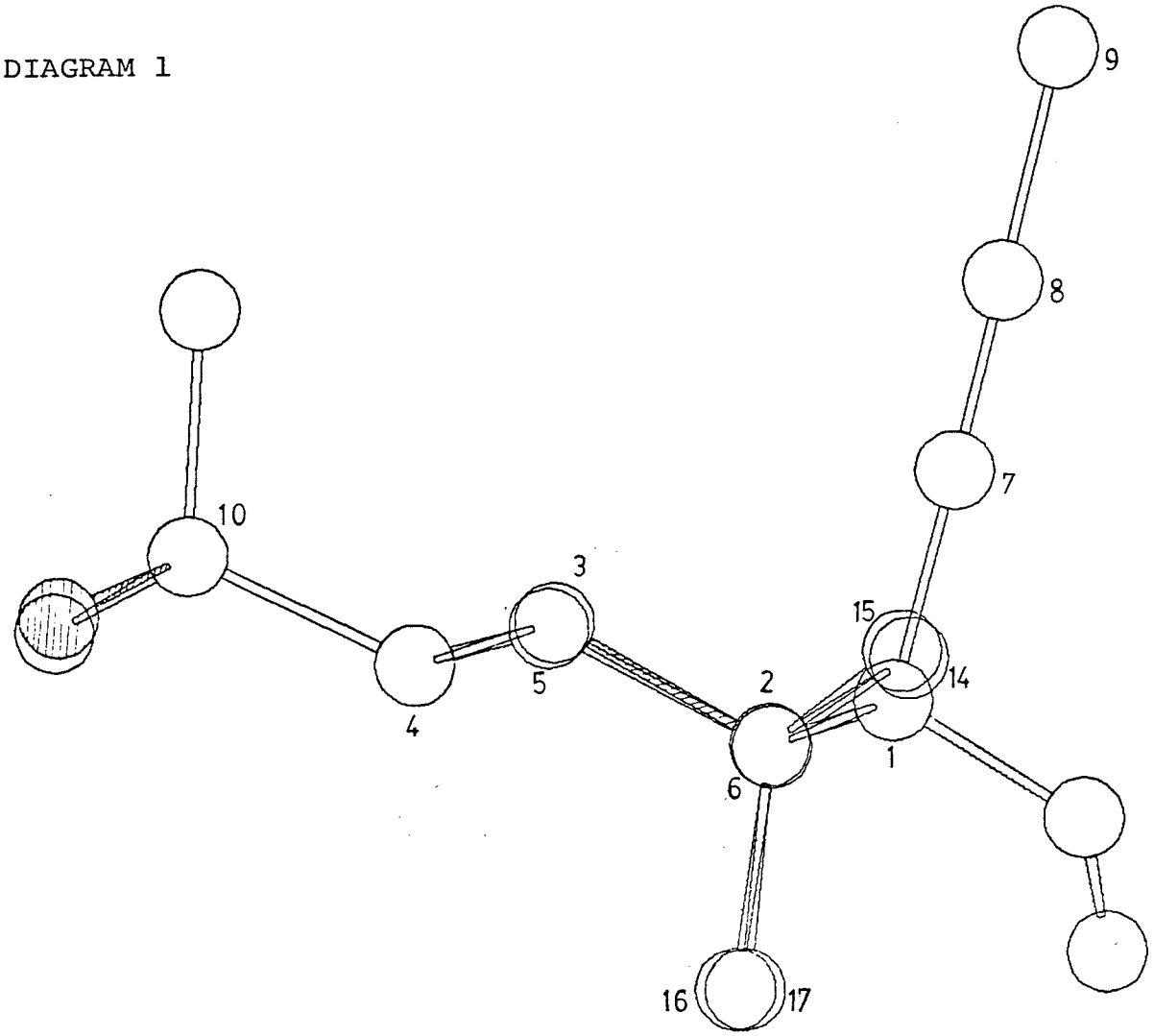
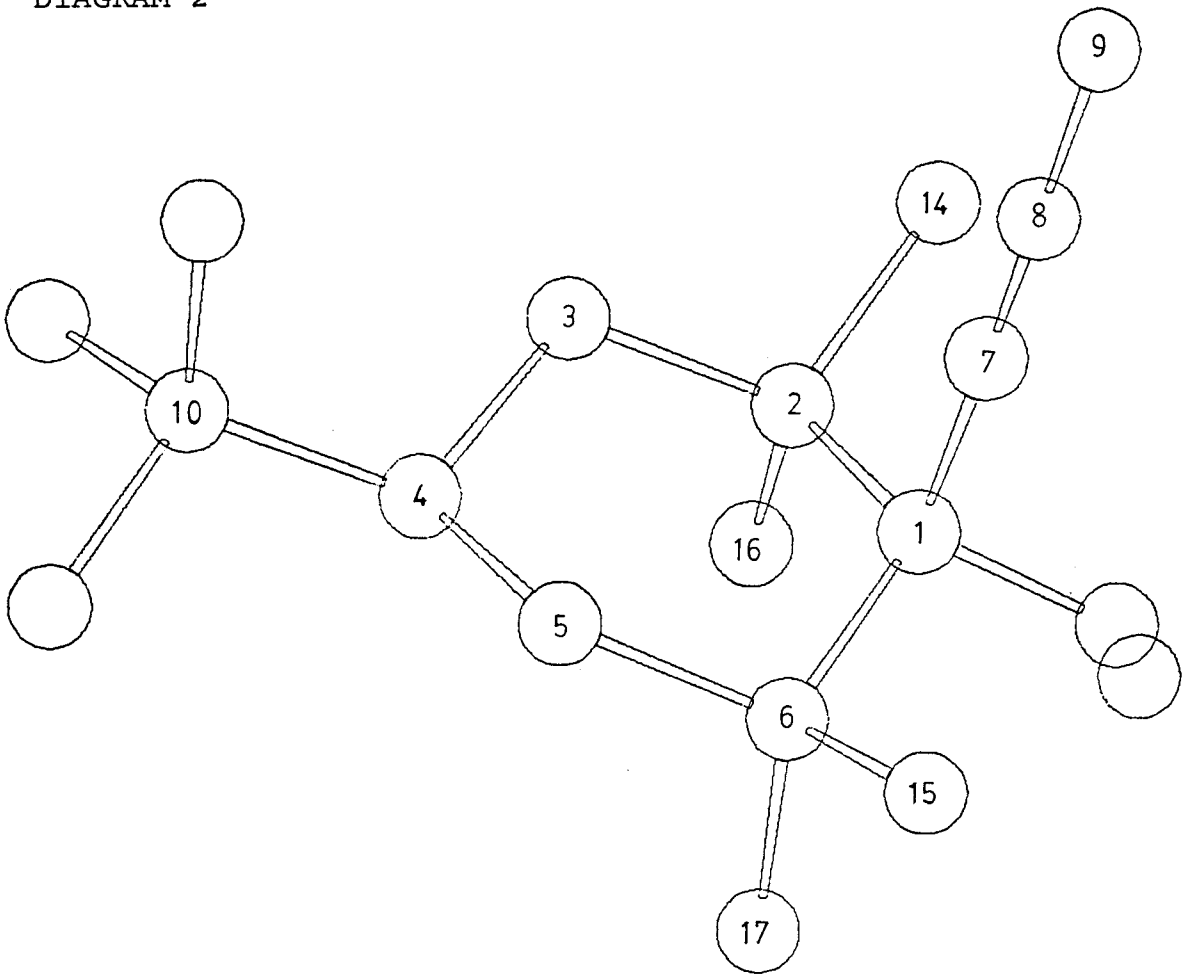


DIAGRAM 2



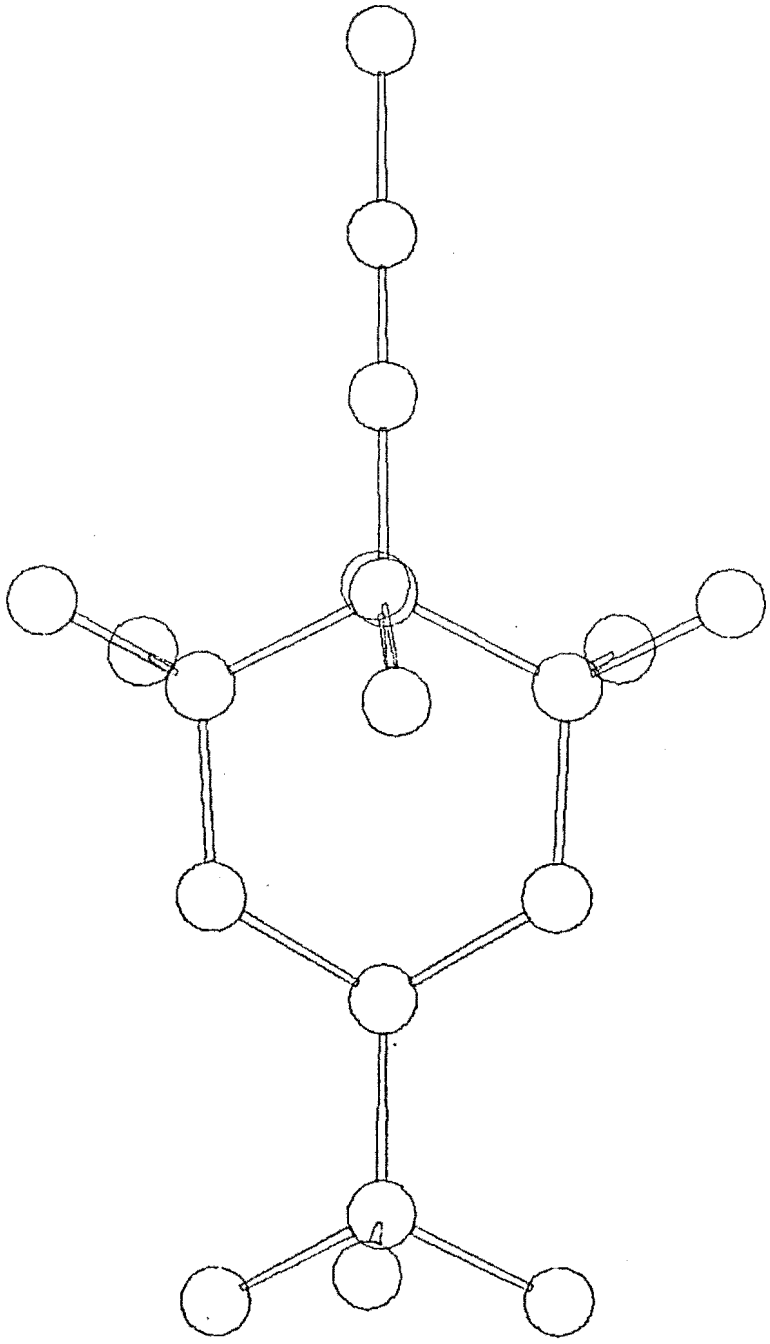


DIAGRAM 3

EXPERIMENTAL

Melting points are uncorrected. Ultraviolet absorptions were determined for cyclohexane solutions on a Shimadzu MPS50L spectrometer. Infrared spectra were recorded on a Shimadzu IR27G spectrophotometer for liquid films or Nujol mulls. ^{1}H n.m.r. spectra were recorded for carbon tetrachloride solutions, with tetramethylsilane as an internal reference, on a Varian T-60 spectrometer. N.m.r. spectral parameters were derived by first-order analysis, and wherever possible confirmed by double-irradiation experiments. ^{13}C n.m.r. spectra were recorded on a Varian CFT20 spectrometer for $CDCl_3$ solutions with $CHCl_3$ and $SiMe_4$ as internal standards. Mass spectra were recorded on an A.E.I. MS902 spectrometer. Micro-analyses were determined at the University of Otago.

The alumina used for column chromatography was La porte Grade H (100-300 mesh) deactivated by the addition of 5% v/v of 10% aqueous acetic acid. Solvents used for chromatography were purified technical grade. Petroleum ether was distilled off phosphorøus pentoxide and ether was distilled off sodium hydride. Petroleum ether refers to the fraction of b.p. 50-70°. All solvents used for reactions were dried by refluxing with lithium aluminium hydride followed by distillation.

PART I

2,2-Dimethyl-3-phenylpropan-3-on-1-ol(1)[23]

A mixture of isobutyrophenone (0.68 mol), paraformaldehyde (0.24 mol), anhydrous potassium carbonate (0.069 mol) and methyl alcohol (117 ml) was stirred at room temperature for 4½ days. It was then poured into 450 ml of water and the resulting mixture was acidifed with concentrated hydrochloric acid. The crude product was extracted with three 80-ml portions of benzene. Distillation of the crude product under reduced pressure (b.p. 115-134/3 mm) gave the hydroxyketone (1) (0.26 mol). From the residue 0.006 mol of (1) was recrystallised from ether/petroleum ether, m.p. 79-81°. Total yield of (1) was 39%. ν_{max} (liquid film) 3455, 1680 cm^{-1}. N.m.r. δ1.30, s, 6H, $C(CH_3)_2$; 2.92, s, OH; 3.55, s, CH_2; 7.20-7.77, m, aromatic protons.

1-Methoxy-2,2-dimethyl-3-phenylpropan-3-one(2)[32]

To a solution of ketone (1) (0.079 mol) in dimethylformamide (200 ml) was added methyl iodide (0.23 mol) and silver oxide (0.15 mol). The resulting mixture was stirred at room temperature for 40 h. The insoluble salts were removed and the crude product was extracted with chloroform. Ketone (2) (0.04 mol, 54% yield) was separated from Ketone (1) by chromatography on 5% deactivated alumina. ν_{max} (liquid film) 1680, 1105 cm^{-1}. N.m.r. δ1.23, s, 6H, $C(CH_3)_2$; 3.22, s, OCH_3; 3.40, s, CH_2; 7.17-7.58, m, 5H, aromatic protons.

PRODUCTION OF PROPYNE.

(i) Propene

Phosphoric acid (80 ml) was heated to 260°-270° and this temperature was maintained while isopropanol (200 ml) was added dropwise. The propene gas (2 moles) was trapped in a tube immersed in dry ice/isopropanol bath.

(ii) 1,2-Dibromopropane

Gaseous propene (2 mol) was bubbled into dried ether (500 ml) at a temperature of -50°C. Bromine (~2 moles) was then added at -40° to -60° with stirring and cooling until the brown colour persisted. The ether was thoroughly removed by a water pump vacuum. Propylene bromide was obtained (1.65 mol, 83% yield) as a colourless liquid.

(iii) Propyne

A solution of potassium hydroxide (51 g) in n-butanol (125 ml) was heated to boiling. This temperature was maintained as the propylene bromide (0.19 mol) was added dropwise and the potash solution was well agitated. The alcohol vapour which passed through the exit tube from the 3-necked flask was removed by a trap cooled in ice. The propyne gas (0.12 mol) was collected in a trap immersed in an isopropyl alcohol/dry ice bath.

Preparation of n-butyllithium

Lithium pieces (1.25 mol) were introduced in a stream of nitrogen to anhydrous ether (200 ml) in a 500 ml 3-necked

flask fitted with a stirrer. n-Butyl bromide (0.11 mol) was added and stirring was started to initiate the reaction. After about 20 min. the rest of the n-butyl bromide (0.39 mol) in ether (75 ml) was added in small portions, keeping the temperature of the solution mixture between -15^{o} to -25^{o}. After addition was complete the reaction mixture (greyish) was allowed to rise gradually to -5^{o} over a period of about 1 h. The reaction mixture then cooled at -20^{o} to -25^{o} and was filtered into a measuring cylinder which has been previously filled with nitrogen. The yield of n-butyllithium was 58%. The strength of the n-butyllithium was determined by the titration method as follows: (1) 5 ml aliquot of the solution was hydrolysed with 10 ml of distilled water. It was then titrated with hydrochloric acid (1M) to determine the total alkali present using phenolphthalein as indicator. (2) A second aliquot of the solution was reacted with a solution of benzyl chloride (1 ml) in anhydrous ether (10 ml). The resulting mixture was allowed to stand for 1 min and then hydrolysed with 10 ml of distilled water. It was then titrated against hydrochloric acid (1M) to determine the alkali present other than the n-butyllithium. The difference between the two titrations values represents the concentration of n-butyllithium.

Propynyllithium

Ether (9 ml), at -30^{o} or lower, was mixed with propyne (9 ml, 1.5 mol) at -70^{o} and poured into a solution of n-butyllithium (0.05 mol) in ether (30 ml), as quickly as possible at -10^{o} or lower temperature in a stream of nitrogen. Stirring was required.

1-Methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7)

1-Methoxy-2,2-dimethyl-3-phenylpropan-3-one (2) (0.03 mol) in ether (30 ml) was added in small portions to the propynyllithium (prepared as above) at -20°, and the resulting mixture was stirred for 18 h at room temperature. It was then hydrolysed with saturated ammonium chloride solution (200 ml) and the crude product was extracted with ether (3 x 300 ml). The alkynol (B7) (7.2 g, 97% yield) was purified by chromatography on 5% deactivated alumina. ν_{max} (liquid film) 3450, 2250 cm^{-1}. N.m.r. δ0.80, s, 3H, C2-$(CH_3)_A(CH_3)_B$; 0.87, s, 3H, C2-$(CH_3)_A(CH_3)_B$; 1.93, s, 3H, $-C\equiv C-CH_3$; 3.13, d, J_{AB} 10 Hz, 1H, Cl-H_AH_B; 3.40, s, methoxy protons; 3.75, d, J_{BA} 9 Hz, 1H, Cl-H_AH_B; 4.27, s, OH; 7.1-7.6, m, 5H, aromatic protons (Found: M^+, 232.1398. Calc. for $C_{15}H_{20}O_2$: M^+, 232.1463). (Found: C77.37; H8.98. $C_{15}H_{20}O_2$ requires C, 77.55; H8.68).

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7) with lithium aluminium hydride in diethyl ether.

(a) Alkynol (B7) (500 mg) in diethyl ether (2 ml) was added to a suspension of lithium aluminium hydride (90 mg) in the same solvent (8 ml). To the resulting mixture was added another volume of diethyl ether (15 ml), and the whole reaction mixture was heated under reflux with stirring in an atmosphere of nitrogen for 16 h. After the addition of water the crude product, isolated by means of ether, was adsorbed onto alumina (50 g).

Elution with petroleum ether gave the 1-methoxy-2,2-dimethyl-3-phenylhexa-3,4-diene (C4) (292 mg). ν_{max} (liquid film) 1965, 1110 cm^{-1}. N.m.r. δ1.07, s, 6H, C2-$(CH_3)_2$; 1.67, d, J 8 Hz, C6-H_3; 3.08, s, CH_2; 3.25, s, OCH_3; 5.09, q, J 8 Hz, 1H, vinylic H; 7.15, s, 5H, aromatic protons (Found: M^+, 216.1418. Calc. for $C_{15}H_{20}O$: M^+, 216.1514). (Found: C, 83.28; H, 9.24. $C_{15}H_{20}O$ requires C, 83.28; H, 9.32).

Elution with petroleum ether and petroleum ether/ether (96:4) gave the (E)-1-methoxy-2,2-dimethyl-3-phenyl-hex-4-en-3-ol (C3) (148 mg). ν_{max} (liquid film) 3500, 1090, 970 cm^{-1}. N.m.r. δ0.85, s, 6H, C2-$(CH_3)_2$; 1.74, d, J 6 Hz, C6-H_3; 2.96, d, J 9 Hz, 1H, C1-H_AH_B; 3.26, d, J 9 Hz, 1H, C1-H_AH_B; 3.27, s, 3H, methoxy protons; 4.07, s, OH; 5.82, dq, $J_{5,4}$ 14 Hz, $J_{5,Me}$ 6 Hz, H5; 6.16, d, $J_{4,5}$ 14 Hz, H4; 7.0-7.4, m, 5H, aromatic protons (Found: $M^+-C_5H_{11}O$, 147.0750. Calc. for $C_{15}H_{22}O_2$: $M^+-C_5H_{11}O$, 147.0810). (Found: C, 76.87; H, 9.58. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46).

Elution with ether gave the alkynol (B7) (38 mg), identical (n.m.r.) with an authentic sample.

(b) The alkynol (B7) was treated in the same manner as above except the excess lithium aluminium hydride was destroyed with deuterium oxide and the crude product, isolated by means of ether, was adsorbed onto 5% deactivated alumina (50 g).

Elution with petroleum ether gave the allene (C4) (283 mg), identical (n.m.r.) with an authentic sample.

Elution with petroleum ether/ether (97:3) gave 4-deutero and 5-deutero (E)-alkenols (C3) (152 mg) as a

mixture (5:27). ν_{max} 3500, 1100, 960, 920, 880 cm^{-1}. N.m.r. (4-deutero) δ0.85, s, 6H, C2-$(Me)_2$; 1.73, d, J 7 Hz, 3H, vinylic CH_3; 2.96, d, J 9 Hz, 1H, CH_AH_B; 3.26, d, J 9 Hz, 1H, CH_AH_B; 3.27, s, 3H, OCH_3; 4.03, s, OH; 5.79, q, J 7 Hz, H5; 7.0-7.4, m, 5H, aromatic protons. N.m.r. (5-deutero) δ0.85, s, 6H, C2-$(Me)_2$; 1.75, s, 3H, vinylic CH_3; 2.96, d, J 9 Hz, 1H, CH_AH_B; 3.26, d, J 9 Hz, 1H, CH_AH_B; 3.27, s, 3H, OCH_3; 4.05, s, OH; 6.17, m, $W_{h/2}$ 6 Hz, H4; 7.0-7.4, m, 5H, aromatic protons.

Elution with the ether gave the alkynol (B7) (33 mg), identical(n.m.r.) with an authentic sample.

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol (B7) with lithium aluminium deuteride in diethyl ether.

Reaction of the alkynol (B7) with lithium aluminium deuteride, as described in (a) above, gave a crude product of which its components were separated by chromatography on 5% deactivated alumina.

5-Deutero allene (C4) (288 mg). ν_{max} (liquid film) 1960, 1105 cm^{-1}. N.m.r. δ1.05, s, 6H, C2-$(CH_3)_3$; 1.65, s, 3H vinylic CH_3; 3.05, s, CH_2; 3.22, s, OCH_3; 7.10, s, 5H, aromatic protons (Found: M^+, 217.1577. Calc. for $C_{15}H_{19}DO$: M^+, 217.1592).

4-Deutero and 5-deutero (E)-alkenols (C3) (116 mg) as a mixture (23:3). Alkynol (B7) (52 mg), identical (n.m.r.) with an authentic sample.

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol with lithium aluminium hydride in tetrahydrofuran.

(a) To a suspension of lithium aluminium hydride

(90 mg) in tetrahydrofuran (8 ml) was added a solution of the alkynol (500 mg) in the same solvent (2 ml). More solvent (15 ml) was added and the resulting mixture was heated at 35° with stirring for 16 h in an atmosphere of nitrogen. The excess lithium aluminium hydride was destroyed with water and the crude product was isolated by means of ether, and subsequently absorbed onto alumina (50 g).

Elution with petroleum ether gave the allene (C4) (110 mg), identical (n.m.r.) with an authentic sample. Elution with petroleum ether/ether (95:5) gave the (E)-alkenol (C3) (357 mg) and further elution with ether gave the starting alkynol (15 mg), both (n.m.r.) were identical with authentic samples of (C3) and (B7) respectively.

(b) The alkynol (B7) was reacted, as above, except the excess lithium aluminium hydride was destroyed with deuterium oxide. Subsequent separation of the crude product by chromatography on alumina gave the following products: allene (C4) (104 mg); 4-Deutero and 5-deutero (E)-alkenols (C3) (357 mg) as a mixture (49:26); and the starting alkynol (31 mg). All were identical (n.m.r.) with authentic samples of (C4), (C3) and (B7) respectively.

(c) The alkynol was added to the lithium aluminium hydride in the same manner as before but the mixture was heated under reflux for 2.5 h in an atmosphere of nitrogen. The excess lithium aluminium hydride was

destroyed with water and the crude product was isolated by means of ether, followed by chromatography on alumina gave: Allene (C4) (270 mg); (E)-alkenol (C3)(187 mg) and alkynol (B7)(13 mg), all of which were identical (n.m.r.) with authentic samples of (C4), (C3) and (B7) respectively.

(d) Reaction of the alkynol was as (c) above but the lithium aluminium hydride was destroyed with deuterium oxide. Subsequent chromatography of the crude product on alumina gave: the allene (C4) (273 mg), the 4-deutero and the 5-deutero (E)-alkenols (C3)(179 mg) as a mixture (16:21), and the starting alkynol (15 mg).

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol with lithium aluminium deuteride in tetrahydrofuran.

(a) The alkynol was reacted with lithium aluminium deuteride, as (a) above, followed by chromatography of the crude product on alumina gave: the 5-deutero allene (C4) (133 mg), the 4-deutero and the 5-deutero (E)-alkenols (C3) (359 mg) as a mixture (30:40), and the alkynol (B7)(7 mg).

(b) The alkynol (B7) was reacted with lithium aluminium deuteride, as (c) above, followed by chromatography of the crude product gave: the 5-deutero allene (259 mg), the 4-deutero and the 5-deutero (E)-alkenols (203 mg) as a mixture (25:17), and the starting alkynol (18 mg).

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol with lithium aluminium deuteride in 2,5-dimethyltetrahydrofuran.

(a) The alkynol (500 mg) in 2,5-dimethyltetrahydrofuran (2 ml) was added to a suspension of lithium aluminium deuteride (100 mg) in 2,5-dimethyltetrahydrofuran (8 ml). More solvent (15 ml) was added to the mixture and it was then heated at 35° with stirring for 16 h in an atmosphere of nitrogen. The excess lithium aluminium deuteride was destroyed with water and chromatography of the crude product on alumina gave: the 5-deutero allene (C4)(239 mg); the 4-deutero and 5-deutero (E)-alkenols (C3)(214 mg) as a mixture (26:18), and an unidentified compound (32 mg).

(b) The alkynol on treatment with lithium aluminium deuteride as above but for 2.5 h at 65° gave the following products by chromatography: the 5-deutero allene (C4) (284 mg); the 4-deutero and 5-deutero (E)-alkenols (C3) (139 mg) as a mixture (23:7), and the starting alkynol (42 mg).

(c) The alkynol on treatment with lithium aluminium deuteride for ½ h under reflux gave, by chromatography on alumina, the products: 5-deutero allene (C4) (342 mg); 4-deutero (E)-alkenol (C3) (126 mg) and the starting material (B7) (10 mg).

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol with lithium aluminium hydride in benzene.

(a) The alkynol (500 mg) in benzene was added to a suspension of lithium aluminium hydride (90 mg) in benzene in the same manner as before, and the mixture was heated under reflux for 1 h. The crude product was isolated by means of ether and its components were separated by chromatography on alumina: allene C4) (116 mg); (E)-alkenol (C3) (36 mg) and the starting alkynol (329 mg). All were identical (n.m.r.) with authentic samples of (C4), (C3) and (B7) respectively.

(b) In the same preparation as above the reaction mixture was heated under reflux for 20 h. Chromatography of the crude product on alumina gave the allene (C4) (273 mg), (E)-alkenol (C3) (66 mg) and the alkynol (B7) (150 mg).

Reaction of 1-methoxy-2,2-dimethyl-3-phenylhex-4-yn-3-ol with lithium aluminium deuteride in benzene.

Alkynol (B7) (500 mg) was treated with lithium aluminium deuteride, as above, in benzene (25 ml). The solution mixture was heated under reflux for 4 h in an atmosphere of nitrogen. It was then hydrolysed with water and its crude produce was extracted with ether. Chromatography of the crude product gave the 5-deutero allene (C4) (109 mg), the 4-deutero and 5-deutero (E)-alkenols (C3) (46 mg) as a mixture (19:7), and the starting alkynol (327 mg).

3-Methoxy-1-phenylpropyl chloride (1.1)[24]

Styrene (104 g) dissolved in CCl_4 (63 ml) was added dropwise over 2 h to a mixture of α-chloromethyl methyl ether (80.5 g), anhydrous zinc chloride (1.2 g) and carbon tetrachloride (63 ml). The whole operation was carried out with stirring and cooling (15° - 20°). Stirring was continued at this temperature for another 2½ h. The contents of the flask were then decomposed with water and the reaction product (bottom layer) was separated and washed with 3% NaOH and with water (two times each). After drying with magnesium sulphate and the solvent removed, distillation gave 128 g of the ether (1.1), an oily liquid, boiling off at 96 - 98.5° (5-6 mm). The yield was 69% based on styrene weight. Lt. B.p.[24] 100 - 101.5° (6 mm).

3-Methoxy -1-phenylpropanol (1.2)[25]

A mixture of 20% aqueous KOH solution (547 ml) and γ-chloro ether (1.1) (109.2 g) was heated under reflux for 12 hr with stirring. The reaction product was extracted with two portions of ether (200 ml). The ether extract was dried and its solvent was removed. Distillation at 102 - 109° (4 mm) gave the alcohol (1.2) (78.7 g, 80% yield). Lt. B.p.[25] 112 - 113° (5 mm), d_4^{20} 1.0460.

1-Methoxy-3-phenylpropan-3-one (1.3)

The alcohol (1.2) (78.7 g) was dissolved in acetone (429 ml, analytical grade) and cooled to 0 - 5° in a 2-l three-necked flask immersed in an ice bath. The oxidation

reagent was prepared by dissolving chromium trioxide (50.1 g) in 72 ml of water followed by slow addition of concentrated (18M) sulfuric acid (44 ml) and 143 ml of water with stirring[26]. It was then cooled to 0 - 5° in an ice bath and was added to the alcohol solution with vigorous stirring at such a rate so that the temperature of the reaction mixture was maintained at about 20°. The stirring was continued for 3 h after the addition was completed.

Sodium metabisulfite was added in small portions until the brown colour of chromic acid disappeared from the upper layer of the two-phase mixture. The top layer was decanted, and the dense, green, lower layer was extracted with 150 ml of petroleum ether. Combination of this extract with the original upper layer caused a separation into two phases. The lower phase was drawn off and added to the original lower phase, which was then extracted with three 120-ml portions of petroleum ether. The extracts were combined, washed successively with two 40-ml portions of saturated sodium chloride, two 40-ml portions of saturated sodium bicarbonate solution, and 40 ml of saturated sodium chloride solution, and dried over magnesium sulphate. The solvent was removed by water aspirator and the residue was distilled under reduced pressure to give the ketone (1.3) (63 g; 81% yield) b.p. 126 - 128° (15 mm). ν_{max} (liquid film) 1690, 1110 cm^{-1}. N.m.r. δ3.06, d, J 7 Hz, 1H, C2-H_aH_b; 3.24, d, J 7 Hz, C2-H_aH_b; 3.30, 3, CH_3; 3.73, t, J 7 Hz, -CH_2-O-CH_3; 7.2 - 8.0, m, 5H, aromatic protons.

1-Methoxy-3-phenylhex-4-yn-3-ol (B4)

In a 500 ml 3-necked round-bottom flask fitted with a reflux condenser, a dropping funnel and a nitrogen gas inlet tube was added magnesium (2.8 g, 0.12 mole) and the whole system was flushed with dried nitrogen for about ½ h. A crystal of iodine and 10 ml of dried tetrahydrofuran was added to cover the magnesium. Ethyl bromide (2 ml) was then added and external heating was required to initiate the reaction. Once the reaction was started, stirring was commenced and the rest of the ethyl bromide (6 ml) in tetrahydrofuran (60 ml) was added dropwise. When the reaction was completed, it was further refluxed for another ½ h.

While the reaction mixture was refluxing, propyne (14 ml, 0.24 mole) was bubbled into it from a trap and the unreacted propyne together with ethane was collected into another trap with inlet from the top of the condenser. When the propyne was completely evaporated (~ 30 min) during slight warming the traps were transposed. The evaporating procedure was repeated and any remaining liquid was quickly poured into the reaction mixture. After three additional repetitions, the mixture was cooled to room temperature. The reaction mixture consisted of two layers, a greyish underlayer and an almost clear upper layer. 2-Methoxy-ethyl-phenyl ketone (1.3) (8.5 g; 0.05 mole) in the THF (50 ml) was then added in small portions at room temperatures, and the mixture was stirred for 42 h. After which time saturated ammonium chloride solution (200 ml) was required

to decompose the product. The crude product was extracted with ether (3 x 100 ml) and fractionating distillation gave the alkynol (B4) [10.0 g; 98% yield based on the ketone (1.3) weight], bp. 132°-134° (3 mm). ν_{max} (liquid film) 3450, 2250 cm^{-1}. N.m.r. δ1.83, s, 3H, C6-H3; 1.88-3.45, m, 2H, C2-H_2; 3.23, s, -OMe; 3.10-3.55, m, 2H, C1-H_2; 3.88, s, OH; 7.0-7.6, m, 5H, aromatic protons (Found: M^+, 204.1029. Calc. for $C_{13}H_{16}O_2$: M^+, 204.1150. Found: C, 76.11; H, 8.13. $C_{13}H_{16}O_2$ requires C, 76.44; H, 7.90).

Reaction of 1-methoxy-3-phenylhex-4-yn-3-ol (B4) with lithium aluminium hydride in diethyl ether.

To the suspension of lithium aluminium hydride (100 mg) in diethyl ether (8 ml) was added the alkynol (B4, 500 mg) in diethyl ether (17 ml) and the mixture was heated under reflux in an atmosphere of nitrogen for 2.75 h. The excess lithium aluminium hydride was destroyed by water and the crude product was extracted with ether. A major portion (460 mg) was resolved into its components by chromatography on 5% deactivated alumina.

Elution with petroleum ether gave 1-methoxy-3-phenylhexa-4,5-diene (C5) (28 mg). ν_{max} (liquid film) 1948, 1112 cm^{-1}. N.m.r. δ1.74, d, J 7 Hz, vinylic CH_3; 2.63, t, J 7 Hz, C1-CH_2; 6.9-7.4, m, 5H, aromatic protons.

Elution with petroleum ether and petroleum ether/ether (98:2) gave (E)-1-methoxy-3-phenylhex-4-en-3-ol (C6) (243 mg). ν_{max} (liquid film) 3500, 1110, 970 cm^{-1}.

N.m.r. δ1.66, d, J 5 Hz, vinylic CH_3; 2.03, t, J 6 Hz, C2-H_2; 3.15, s, OCH_3; 3.05-3.50, m, C1-H_2; 3.70, s, OH; 4.98-6.25, ABq, 2H, vinylic protons; 7.0-7.4, m, 5H, aromatic protons (Found: M^+, 206.1342. Calc. for $C_{13}H_{18}O_2$: M^+, 206.1307). Found: C, 75.46; H, 9.10. $C_{13}H_{18}O_2$ requires C, 75.69; H, 8.80).

Further elution with petroleum ether/ether (98:2) and (97:3) gave the starting alkynol (B4) (152 mg) identical (n.m.r.) with an authentic sample. Finally elution with ether gave an unidentified compound (25 mg).

Reaction of 1-methoxy-3-phenylhex-4-yn-3-ol with lithium aluminium deuteride in diethyl ether.

The reaction of the alkynol was carried out in the same manner as above except with lithium aluminium deuteride. The crude product was isolated by means of ether and was adsorbed onto alumina (50 g).

Elution with petroleum gave 6-deutero allene (33 mg). ν_{max} (liquid film) 1940,1112 cm^{-1}. N.m.r. δ1.75, s, vinylic CH_3; 2.60, t, J 7 Hz, C2-CH_2; 3.27, s, OCH_3; 3.45, t, J 7 Hz, C1-CH_2; 6.9-7.4, m, 5H, aromatic protons (Found M^+, 189.1264. Calc. for $C_{13}H_{15}DO$: M^+, 189.1279).

Elution with petroleum ether and petroleum ether/ether (98:2) gave a mixture (48:25) of 4-deutero and 5-deutero (E)-alkenols (C6) (275 mg). N.m.r. (4-deutero) δ1.68, d, J 6 Hz, vinylic CH_3; 2.05, t, J 6 Hz, C2-H_2; 3.22, s, OCH_3; 3.10-3.50, m, C1-H_2; 3.60, s, OH; 5.63, m, $W_{h/2}$ 8 Hz, H5; 6.93-7.47, m, 5H, aromatic protons. N.m.r. (5-deutero) δ1.68, s, vinylic CH_3; 2.05, t, J 6 Hz, C2-H_2; 3.22, s, OCH_3; 3.10-3.50, m, C1-H_2; 3.60, s, OH; 5.63, m, $W_{h/2}$ 8 Hz, H4; 6.93-7.47, m, 5H, aromatic protons.

Elution with petroleum ether/ether (98:2) and petroleum ether/ether (95:5) gave the starting alkynol (128 mg) identical (n.m.r.) with an authentic sample. Finally elution with ether gave an unidentified component (37 mg).

Reaction of 1-methoxy-3-phenylhex-4-yn-3-ol with lithium aluminium hydride in tetrahydrofuran.

(a) The alkynol (B4) (500 mg) in tetrahydrofuran (17 ml) was added to a suspension of lithium aluminium hydride (100 mg) in the same solvent (8 ml). The temperature of the reaction mixture was maintained at 20° with stirring for 1 h at an atmosphere of nitrogen. It was then hydrolysed with water and extraction with ether gave a crude product which was adsorbed onto 5% deactivated alumina (56 g).

Elution with petroleum ether gave a compound (19 mg) which was not identified. Further elution gave the (E)-alkenol (C6) (193 mg), identical (n.m.r.) with an authentic sample.

Elution with petroleum ether and petroleum ether/ether (95:5) gave the starting material (B4) (216 mg) identical with an authentic sample. Finally elution with ether gave an unidentified compound (15 mg).

(b) The alkynol (2 g) was treated as above with lithium aluminium hydride (400 mg) in tetrahydrofuran

(100 ml). The reaction mixture was heated under reflux for 4 h and the crude product, isolated by means of ether, was adsorbed onto alumina (200 g).

Elution with petroleum ether gave the cyclopropane derivative (C8) (133 mg). ν_{max} (liquid film) 1600, 1495, 970 cm^{-1}. λ_{max} 209 nm (ε8370). N.M.R. δ0.75-1.00, m, 4H, cyclopropane protons; 1.58, d, J 5 Hz, CH_3; 4.96, dq, $J_{2,Me}$ 5 Hz, $J_{2,1}$ 16 Hz, H2; 5.28, d, J 16 Hz, H1; 7.1, s, 5H, aromatic protons (Found: M^+, 158.1085. Calc. for $C_{12}H_{14}$: M^+, 158.1095).

Elution with petroleum ether/ether (98:2) gave the dimer (C7) (334 mg). ν_{max} (liquid film) 1600, 1495, 1110 cm^{-1}. λ_{max} 224 nm (ε19454), 256 nm (ε10000). N.m.r. δ1.13, s, 4H, cyclopropane protons; 1.13, d, J 7 Hz, C5-CH_3; 1.75, d, J 6 Hz, C7-CH_3; 2.5-2.71, m, C2-H_2; 3.03-3.27, obs., C1-CH_2; 3.13, s, OCH_3; 3.47, dq, $J_{5,4}$ 10 Hz, $J_{5,Me}$ 7 Hz, H5; 5.48, d, J 10 Hz, H4; 5.67, q, J 7 Hz, H7; 7.08, s, 10H, aromatic protons (Found: c, 86.78; H,8.88. $C_{25}H_{30}O$ requires C, 86.66; H,8.73).

Elution with petroleum ether/ether (95:5), (93:7), (90:10) gave 3 unidentified compounds (45 mg), (48 mg) and (100 mg) respectively. Final elution with petroleum ether/ether (70:30) gave the (E)-alkenol (C6) (1088 mg) identical with an authentic sample.

Reaction of 1-methoxy-3-phenylhex-4-yn-3-ol with lithium aluminium deuteride in tetrahydrofuran.

(a) The alkynol (500 mg) in tetrahydrofuran (17 ml) was added to a suspension of lithium aluminium deuteride

(115 mg) in tetrahydrofuran (8 ml) and the mixture was stirred for 3 h at 20° in an atmosphere of nitrogen. The excess lithium aluminium deuteride was destroyed with water and the crude product was isolated by means of ether, followed by chromatography on alumina gave: 4-Deutero and 5-deutero (E)-alkenols (C6) (408 mg) as a mixture (48:25); and two unidentified compounds (25 mg) and (39 mg).

(b) The alkynol (500 mg) was treated as above except the reaction mixture was heated under reflux for 17 h. Chromatography of the crude product gave:

(i) 1,2-Dideutero cyclopropane derivative (C8) (16 mg). N.m.r. δ0.75-1.00, m, 4H, cyclopropane protons; 1.57, s, CH_3; 7.1, s, 5H, aromatic protons.

(ii) 4,5,7-Trideutero dimer (C7) (93 mg). N.m.r. δ1.13, s, 7H, cyclopropane protons and C5-CH_3; 1.73, s, C7-CH_3; 2.45-270, m, C2-CH_2; 3.0-3.26, obs., C1-H_2; 3.13, s, OCH_3; 7.08, s, 10H, aromatic protons.

(iii) 4-Deutero (E)-alkenol (C6) (241 mg) identical (n.m.r.) with an authentic sample.

(iv) Two unidentified compounds (33 mg) and (56 mg).

PART II EXPERIMENTAL

4-α-t-Butyl-1-β-propynyl- and 4-α-t-butyl-1-α-propynyl-cyclohexan-1-ols, (B8) and (B11).

The method of preparation for the alkynols (B8 and B11) was similar to that described in Part I for the preparation of 1-methoxy-3-phenylhex-4-yn-3-ol. 4-t-Butyl-cyclohexanone (15 g; 0.1 mole) in ether (90 ml) was added in small portions to the propynylmagnesium bromide prepared by bubbling propyne (30 ml; 0.51 mole) into ethyl magnesium bromide solution [made from magnesium (4 g) and ethyl bromide (15 ml) in ether (160 ml)]. The reaction mixture was stirred at room temperature for 30 h, after which time it was poured into saturated ammonium chloride solution (300 ml). The crude product was isolated by means of ether (2 x 150 ml) and subsequently was adsorbed onto 5% deactivated alumina (850 g).

Elution with petroleum ether/ether (98:2) and (90:10) gave two oily products (0.19 g) and (1.4 g), the structures of which were not identified.

Elution with petroleum ether/ether (88:12) gave the 4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B8) (2.65 g, 14% yield). Recrystallisation from petroleum ether gave crystalline material, mp. 90-92°. ν_{max} (nujol mull) 2425, 2240 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 1.27, s, OH; 1.0-2.3, m, 9H, cyclohexyl protons; 1.78, s, $C\equiv C-CH_3$ (Found: M^+, 194.1671. Calc. for $C_{13}H_{22}O$: M^+, 194.1671. Found: C, 79.96; H, 11.14. $C_{13}H_{22}O$ requires C, 80.35; H, 11.41).

Elution with petroleum ether/ether (80:20) gave the 4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B11) (13.68 g, 70% yield), mp. 73-74°. ν_{max} (nujol mull) 3275, 2240 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.9-2.3, m, 9H, cyclohexyl protons; 1.83, s, $C\equiv C-CH_3$; 1.90, s, OH (Found: M^+, 194.1698. Calc. for $C_{13}H_{22}O$: M^+, 194.1671. Found: C, 80.08; H, 11.47. $C_{13}H_{22}O$ requires C, 80.35; H, 11.41).

Reaction of alkynol (x)* with lithium aluminium hydride (deuteride) in an ether solvent.

General method: The total volume of an ether solvent used was 5 ml to every 100 mg of reacting alkynol (x). To a suspension of lithium aluminium hydride (deuteride) (1.1 molar equivalents) in the ether solvent was added the alkynol (x) in the same solvent at a rate so that the evolution of hydrogen was not vigorous. The reaction mixture was either stirred at a certain temperature or heated under reflux with stirring for a specific period of time in an atmosphere of nitrogen. The excess lithium aluminium hydride (deuteride) was destroyed with water or deuterium oxide. Sodium potassium tartrate was added to dissolve the aluminium gel that was formed and the crude product was extracted with ether twice. The ether solution was washed with water and dried over magnesium sulphate. The ether solvent was then taken off with water aspirator.

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* (x) can be any one of the compounds, (B8-15).

Reduction of 4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B8) with lithium aluminium hydride in diethyl ether.

(a) See general method for experimental procedure above. The reaction was carried out in diethyl ether at 35° for 24 h with alkynol (B8) (400 mg) and lithium aluminium hydride (92 mg). The crude product was adsorbed onto alumina (100 g).

Elution with petroleum ether gave trans*-allene (D1) (23 mg). ν_{max} (liquid film) 1970 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.9-2.5, m, 9H, cyclohexyl protons; 1.61, d, J 7 Hz, C9-H_3; 4.78, ddq, $J_{H8,Me}$ 7 Hz, $J_{H8,\beta-H2}$ 3.5 Hz, $J_{H8,\beta-H6}$ 3.5 Hz, H8 (Found: C, 87.25; H, 12.39. $C_{13}H_{22}$ requires C, 87.56; H, 12.44).

Elution with petroleum ether/ether (94:6) gave 4-α-t-butyl-1-β-(Z)-propenylcyclohexan-1-ol (D2) (10 mg). ν_{max} (liquid film) 3450, 710 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.7-1.7, (s,m), 10H, (OH, cyclohexyl protons); 1.83, d, J 5 Hz, CH_3; 5.0-5.6, ABq, 2H, vinylic protons (Found: M^+, 196.1830. Calc. for $C_{13}H_{24}O$: M^+, 196.1827).

Further elution with petroleum ether/ether (93:7) gave 4-α-t-butyl-1-β-(E)-propenylcyclohexan-1-ol (D3) (25 mg), mp. 100-101.5°. ν_{max} (nujol mull) 3360, 965 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 1.06, s, OH; 1.1-1.6, m, 9H, cyclohexyl protons; 1.66, d, J 5 Hz, CH_3; 5.43, d, $J_{7,8}$ 15 Hz, H7; 5.66, dq, $J_{8,Me}$ 5 Hz, $J_{8,7}$ 15 Hz, H8 (Found: M^+, 196.1825. Calc. for $C_{13}H_{24}O$: M^+, 196.1827. Found: C, 79.49; H, 12.67. $C_{13}H_{24}O$ requires C, 79.53; H, 12.32).

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* Refer to t-butyl group and C8-CH_3.

Finally, elution with petroleum ether/ether (80:20) gave the starting alkynol (B8) (333 mg) identical (n.m.r.) with an authentic sample.

(b) The reaction of the alkynol (B8) (400 mg) with lithium aluminium hydride (92 mg) was carried out at 35° for 96 h. Chromatography of the crude product on alumina (95 g) gave: Allene (D1) (116 mg); (Z)-alkenol (D2) (13 mg); (E)-alkenol (D3) (52 mg) and the starting alkynol (B8) (187 mg). The four samples were identical (n.m.r.) with authentic samples of (D1), (D2), (D3) and (B8) respectively.

Reduction of 4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B8) with lithium aluminium deuteride in diethyl ether (refer to general method).

Reaction of alkynol (B8) (400 mg) with lithium aluminium deuteride (101 mg) as (b) above gave a crude product the components of which were separated by chromatography on alumina (90 g).

8-Deutero allene (D1) (68 mg). ν_{max} (liquid film) 1970 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.9-2.8, m, 9H, cyclohexyl protons; 1.63, s, C9-H_3.

7-Deutero (Z)-alkenol (D2) (7 mg). N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.7-1.7, (s,m), 10H (OH, cyclohexyl protons); 1.83, d, J 7 Hz, C9-H_3; 5.34, qt, $J_{8,Me}$ 7 Hz, $J_{8,D}$ 3 Hz, H8 (Found: M^+ 197.1889. Calc. for $C_{13}H_{23}DO$: M^+, 197.1892).

7-Deutero and 8-deutero (E)-alkenols (D3) (32 mg) (16:10 -mixture). N.m.r. (7-deutero) δ0.83, s, 9H, $C(CH_3)_3$; 1.0-1.6, m, 9H, cyclohexyl protons; 1.53, s, OH; 1.63, d, $J_{Me,8}$ 6 Hz, C9-H_3; 5.45, m, H8. N.m.r. (8-deutero) δ0.83, s, 9H, $C(CH_3)_3$; 1.0-1.6, m, 9H, cyclohexyl protons; 1.53, s, OH; 1.63, s, C9-CH_3; 5.60, m, H7.

Alkynol (B8) (279 mg) identical (n.m.r.) with an authentic sample.

Reaction of 4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B8) with lithium aluminium hydride in tetrahydrofuran (refer to general method).

Reaction of the alkynol (400 mg) with lithium aluminium hydride (92 mg) in tetrahydrofuran at 65° for 5 h gave a crude product the components of which were separated by chromatography on alumina (90 g): Allene (D1) (66 mg), (E)-alkenol (D3) (261 mg) and the starting alkynol (B8) (34 mg) all of which were identical (n.m.r.) with authentic samples of (D1), (D3) and (B8) respectively.

Reaction of 4-α-t-butyl-1-β-propynylcyclohexan-1-ol with lithium aluminium deuteride in tetrahydrofuran (refer to general method).

Reaction of the alkynol (400 mg) with lithium aluminium deuteride (101 mg) as above gave 8-deutero allene (D1) (64 mg), 7-deutero and 8-deutero (E)-alkenols (D3) (251 mg) as a mixture (53:17), and the alkynol (B8) (50 mg).

Reaction of 4-α-t-butyl-1-β-propynylcyclohexan-1-ol with lithium aluminium hydride in 2,5-dimethyltetrahydrofuran (refer to general method).

(a) Reaction of the alkynol (B8) (400 mg) with lithium aluminium hydride (92 mg) in 2,5-dimethyltetrahydrofuran (25 ml) was carried out at 65°/5.5 h, and chromatography of the crude product on alumina gave: Allene (D1) (98 mg); (Z)-alkenol (D2) (27 mg); (E)-alkenol (D3) (165 mg) and the starting alkynol (58 mg). The four compounds were identical (n.m.r.) with authentic samples of (D1), (D2), (D3) and (B8) respectively.

(b) The reaction of the alkynol (400 mg) was carried out as above except the reaction mixture was heated under reflux for 1 h. The products were: Allene (D1) (233 mg); (Z)-alkenol (D2) (14 mg); (E)-alkenol (D3) (66 mg) and the starting alkynol (14 mg).

Reaction of 4-α-t-butyl-1-β-propynylcyclohexan-1-ol with lithium aluminium deuteride in 2,5-dimethyltetrahydrofuran (refer to page 120).

(a) Reaction of the alkynol (400 mg) with lithium aluminium deuteride (101 mg) as (a) above gave a crude product the components of which were separated by chromatography on alumina (90 g): (1) 8-Deutero allene (D1) (104 mg) identical (n.m.r.) with an authentic sample. (2) 7-Deutero (Z)-alkenol (D2) (27 mg) identical (n.m.r.) with an authentic sample. (3) 7-Deutero and 8-deutero (E)-alkenols (D3) (166 mg) as a mixture (8:39). (4) Alkynol

(B8) (49 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of the alkynol (400 mg) with lithium aluminium deuteride (101 mg) as (b) above gave a crude product the components of which were separated by chromatography on alumina: (1) 8-Deutero allene (D1) (257 mg). (2) 7-Deutero (Z)-alkenol (D2) (14 mg). (3) 7-Deutero and 8-deutero (E)-alkenols (D3) as a mixture (7:6). (4) Starting alkynol (23 mg).

Reaction of 4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B11) with lithium aluminium hydride in diethyl ether (refer to page 120).

(a) Reaction of alkynol (B11) (500 mg) with lithium aluminium hydride (114 mg) at 35°/23 h in diethyl ether gave a crude product which was adsorbed onto alumina (90 g).

Elution with petroleum ether gave cis*-allene (D4) (18 mg). ν_{max} (liquid film) 1970 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.9-2.5, m, 9H, cyclohexyl protons; 1.58, d, J 7 Hz, C9-H_3; 4.82, ddq, $J_{8,Me}$ 7 Hz, $J_{8,\beta-H2}$ 3.5 Hz, $J_{8,\beta-H6}$ 3.5 Hz, H8 (Found: M^+, 178.1712. Calc. for $C_{13}H_{22}$: M^+, 178.1721. Found: C, 87.25; H, 12.39. $C_{13}H_{22}$ requires C, 87.56; H, 12.44).

Elution with petroleum ether/ether (85:15) gave 4-α-t-butyl-1-α-(Z)-propenylcyclohexan-1-ol (D5) (16 mg), mp. 84-86°. ν_{max} (nujol mull) 3300-3360, 1655, 710 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.9-2.2, (s,m), 10H, (OH, cyclohexyl protons); 1.88, d, J 5 Hz, C9-H_3; 5.0-6.1,

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* Refer to t-butyl group and C8-CH_3.

ABq, 2H, vinylic protons (Found: M^+, 196.1750. Calc. for $C_{13}H_{24}O$: M^+, 196.1827. Found: C, 79.47; H, 12.51. $C_{13}H_{24}O$ requires C, 79.53; H, 12.32).

Elution with petroleum ether/ether (70:30) gave 4-α-t-butyl-1-α-(E)-propenylcyclohexan-1-ol (D6) (274 mg), mp. 80-82.5°. ν_{max} (nujol mull) 3340, 1670, 970 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.9-2.0, (s,m), 10H, (OH, cyclohexyl protons); 1.69, d, J 5 Hz, C9-H_3; 5.4-5.8, ABq, 2H, vinylic protons (Found: M^+, 196.1802. Calc. for $C_{13}H_{24}O$: M^+, 196.1827. Found: C, 79.24; H, 12.71. $C_{13}H_{24}O$ requires C, 79.53; H, 12.32).

Finally, elution with petroleum ether/ether (50:50) gave the starting alkynol (B11) (173 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of the alkynol (B11) (500 mg) as above but for 45 h followed by chromatography on alumina (90 g) gave: Allene (D4) (29 mg); (Z)-alkenol (D5) (18 mg); (E)-alkenol (D6) (327 mg) and the starting alkynol (B11) (116 mg). The four compounds were identical (n.m.r.) with authentic samples of (D4), (D5), (D6) and (B11) respectively.

(c) Reaction of the alkynol (B11) (500 mg) as (a) above but for 96 h followed by chromatography on alumina (90 g) gave: allene (D4) (36 mg); (Z)-alkenol (D5) (33 mg); (E)-alkenol (D6) (356 mg) and the starting alkynol (B11) (62 mg).

(d) Reaction of the alkynol (B11) (500 mg) with lithium aluminium hydride (114 mg) as (c) above but worked up with deuterium oxide (3 ml) gave a crude product the components of which were separated by chromatography on alumina (80 g).

cis-Allene (D4) (35 mg) identical (n.m.r.) with an authentic sample.

8-Deutero (Z)-alkenol (D5) (41 mg). N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.6-2.1, (s,m), 10H, (OH, cyclohexyl protons); 1.86, s, C9-H_3; 5.52, m, $W_{h/2}$ 6 Hz, H7.

8-Deutero (E)-alkenol (D6) (360 mg). N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.6-2.0, (s,m), 10H, (OH, cyclohexyl protons); 1.70, s, C9-H_3; 5.57, m, $W_{h/2}$ 6 Hz, H7.

Alkynol (B11) (37 mg) identical (n.m.r.) with an authentic sample.

Reaction of 4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B11) with lithium aluminium deuteride in diethyl ether (refer to page 120).

(a) Reaction of the alkynol (B11) (500 mg) with lithium aluminium deuteride (126 mg) in diethyl ether (25 ml) as (b) above gave a crude product the components of which were separated by chromatography on alumina (90 g).

8-Deutero cis-allene (D4) (22 mg). N.m.r. δ 0.83, s, 9H, $C(CH_3)_3$; 0.9-2.6, m, 9H, cyclohexyl protons; 1.57, s, C9-H_3.

7-Deutero (Z)-alkenol (D5) (11 mg), mp. 84-86°. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.9-2.0, (s,m), 10H, (OH,

cyclohexyl protons; 1.86, d, J 7 Hz, C9-H_3; 5.51, qt, $J_{8,Me}$ 7 Hz, $J_{8,D}$ 2 Hz, H8.

7-Deutero (E)-alkenol (D6) (252 mg), mp. 80-82.5°. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.9-2.0, (s,m), 10H, (OH, cyclohexyl protons); 1.72, d, J 6 Hz, C9-H_3; 5.63, m, H8.

Alkynol (B11) (204 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of the alkynol (B11) (500 mg) with lithium aluminium deuteride (126 mg) as (c) above followed by chromatography on alumina gave: 8-Deutero cis-allene (D4) (35 mg); 7-deutero (Z)-alkenol (D5) (33 mg); 7-deutero (E)-alkenol (D6) (366 mg) and the starting alkynol (B11) (43 mg), each of which was identical (n.m.r.) with an authentic sample.

Reaction of 4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B11) with lithium aluminium hydride in tetrahydrofuran (refer to page 120).

Alkynol (B11) (500 mg) was heated under reflux with lithium aluminium hydride (114 mg) for 23 h in tetrahydrofuran (25 ml). Chromatography of the crude product gave the allene (D4) (81 mg), the (Z)-alkenol (D5) (22 mg) and the (E)-alkenol (D6) (349 mg).

Reaction of 4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B11) with lithium aluminium deuteride in tetrahydrofuran (refer to page 120).

Alkynol (B11) (500 mg) was reacted in the same

conditions as above but with lithium aluminium deuteride (126 mg). Chromatography of the crude product on alumina gave: 8-Deutero allene (D4) (69 mg); 7-deutero (Z)-alkenol (D5) (20 mg) and 7-deutero (E)-alkenol (D6) (383 mg), each of which was identical (n.m.r.) with an authentic sample.

Reaction of 4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B11) with lithium aluminium hydride in 2,5-dimethyltetrahydrofuran (refer to page 120).

Reaction of the alkynol (500 mg) with lithium aluminium hydride (114 mg) in 2,5-dimethyltetrahydrofuran (25 ml) was carried out at 91°/10 h, and chromatography of the crude product on alumina gave the allene (D4) (154 mg), the (Z)-alkenol (D5) (14 mg) and the (E)-alkenol (D6) (274 mg).

Reaction of 4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B11) with lithium aluminium deuteride in 2,5-dimethyltetrahydrofuran (refer to page 120).

Reaction of the alkynol (500 mg) with lithium aluminium deuteride (126 mg) as above followed by chromatography of the crude product on alumina gave the 8-deutero allene (D4) (167 mg), the 7-deutero (Z)-alkenol (D5) (11 mg) and the 7-deutero (E)-alkenol (D6) (244 mg).

Ethyl 4-t-butyl-1-cyclohexanone-2-carboxylate (2.1)[27]

Sodium (29.8 g, 1.3 mol) was dissolved in dry ethanol (400 ml) in a 2-ℓ 3-neck flask equipped with a stirrer, a dropping funnel, and a condenser carrying a

drying tube. The flask was immersed in an ice-salt bath and the stirrer was started. When the temperature of the solution had reached 10°, an ice-cold solution of 4-t-butylcyclohexanone (200 g, 1.3 mol) and ethyl oxalate (190 g, 1.4 mol) in dry ethanol (200 mol) was added during 30 min. The ice bath was retained for 10 h, and then the red solution was stirred at room temperature for 6 h. After which time it was decomposed by careful addition of ice-cold dilute sulphuric acid prepared by the addition of concentrated acid (36 ml) to ice (320 g). During this neutralization the temperature of the mixture was maintained at 5-10°. The mixture was then diluted with cold water to a volume of about 3 ℓ, and the heavy oil that separated was removed. The aqueous phase was extracted with benzene (2 x 200 ml). The heavy oil was combined with the extracts, and the resulting solution was washed with water, and the benzene was removed by means of a water aspirator. The pale red liquid residue was then heated under reflux with 1 g of glass wool and a trace of iron powder for 8 h. The residue was fractionally distilled through a 2-ft Vigreux column. Distillation at 71°-82° (2.2 mm) gave the ethyl oxalate and 4-t-butylcyclohexanone as a mixture (64 g). Distillation at 110°-134° (6-7.5 mm) gave a mixture of 4-t-butylcyclohexanone and the keto ester (2.1) (5 g). Finally, distillation at 134°-138° (7-8 mm) gave the keto ester (2.1) (168 g, 54% based on the weight of 4-t-butylcyclohexanone used).

Cis- and trans-2-methyl-4-t-butyl-1-cyclohexanone (2.2) and (2.3)[28]

Potassium (27 g) was dissolved in anhydrous tert-butyl alcohol (620 ml) over 3 h in an atmosphere of nitrogen. Keto ester (2.1) (149 g) was then added over 20 min. at room temperature and the mixture was stirred for 1 h. After which time methyl iodide (140 g, 61.6 ml) was added dropwise and the reaction mixture was heated under reflux for 1.5 h with stirring. The mixture was poured into a saturated solution of sodium chloride, and extracted with ether. The extract was dried with magnesium sulphate and distilled. A pale yellow liquid of ethyl 2-methyl-4-t-butyl-1-cyclohexanone-2-carboxylate (2.0) (147.5 g, 93% yield) was obtained; b.p. 93-96^{o} (0.2 mm).

A solution of the keto ester (2.0) (147.5 g) in methanol (404 ml) was boiled with 10% aqueous sodium hydroxide solution (600 ml) for 14 h. The reaction mixture was poured into water and extracted with hexane. The extract was washed with water, dried with magnesium sulphate, and distillation give a mixture of the cis and trans-ketones (2.2 and 2.3) [99.4 g, 96% yield based on keto ester (2.0)]; b.p. 94-96^{o} (10 mm).

Cis-2-methyl-4-t-butyl-1-cyclohexanone (2.2)[29]

To a solution of a mixture of cis and trans-ketones (2.2 and 2.3)(26 g, 0.15 mol) in anhydrous benzene (600 ml), while cooling with ice, was added the dimethyl-amine (24 ml, 0.36 mol) in anydrous benzene (60 ml). A solution of titanium tetrachloride (9 ml) in benzene

(145 ml) was added dropwise while stirring, keeping the temperature between 0-10°. The brown precipitate solution was stirred for 2 h, while being cooled with ice, and for 16 h at 20°. It was then acidified and the benzene solution was removed and extracted with ether (2 x 300 ml). The extract together with the benzene solution was washed with water, dried with magnesium sulphate, and distillation gave the stereoisomeric ketones (2.2 and 2.3)(10.5 g). The acidic aqueous solution was made alkaline with sodium hydroxide solution, and extracted with ether (4 x 300 ml). The extract was washed with water and dried with magnesium sulphate. The solvent was removed, and N,N-dimethyl-N-(2-methyl-4-t-butyl-1-cyclohexen-1-yl) amine (2.5) (15 g, 51% yield) was obtained.

A solution of the amine (2.5)(15 g) in tetrahydrofuran (52 ml) and 3% hydrochloric acid (157 ml) was boiled for 4 hr. The reaction mixture was extracted with ether (3 x 200 ml), washed with water and dried with magnesium sulphate. Distillation gave the cis-ketone (2.2) (10.9 g, 78% yield); b.p. 106-110° (16 mm).

2-α-Methyl-4-α-t-butyl-1-β-propynyl- and 2-α-methyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ols (B9 and B12).

2-α-Methyl-4-α-t-butylcyclohexan-1-one (2.2) (10.9 g, 0.065 mol) in ether (70 ml) was added in small portions to the propynyllithium, prepared as in part I from propyne (0.2 mol) and n-butyllithium (0.1 mol) in ether (250 ml), at -20° and the resulting mixture was stirred for 42 h at room temperature. The whole mixture was then poured into

saturated ammonium chloride solution (130 g of NH_4Cl in 600 ml of H_2O) and the crude product, isolated by means of ether, was adsorbed onto 5% deactivated alumina (800 g).

Elution with petroleum ether/ether (90:10) gave the starting ketone (2.2) (675 mg).

Elution with petroleum ether/ether (85:15) gave 2-α-methyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B9) (3.9 g, 29% yield), mp. 58-60°. ν_{max} (nujol mull) 3500, 2240 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 1.03, d, J 6 Hz, C2-CH_3; 0.8-2.2, m, 8H, cyclohexyl protons; 1.27, s, OH; 1.80, s, C9-H_3 (Found: C, 80.78; H, 11.89. $C_{14}H_{24}O$ requires C, 80.71; H, 11.61).

Elution with petroleum ether/ether (80:20) gave 2-α-methyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B12) (5.7 g, 42% yield), mp. 39-41°. ν_{max} (nujol mull) 3425, 2230 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.93, d, J 6 Hz, C2-CH_3; 1.0-2.0, m, 8H, cyclohexyl protons; 1.80, s, OH; 1.85, s, C9-H_3 (Found: C, 80.78; H, 11.89. $C_{14}H_{24}O$ requires C, 80.71; H, 11.61).

Reaction of 2-α-methyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B9) with lithium aluminium hydride in diethyl ether (refer to page 120).

(a) The mixture of alkynol (B9) (400 mg) and lithium aluminium hydride (80 mg) in diethyl ether (20 ml) was heated under reflux for 97 h. The crude product, isolated by means of ether, was adsorbed onto 5% deactivated alumina (40 g).

Elution with petroleum ether gave trans*-allene (D7)

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* Refer to 4-t-butyl group and C8-CH_3.

(66 mg). ν_{max} (liquid film) 1970 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.93, d, J 6 Hz, C2-CH_3; 1.0-2.6, m, 8H, cyclohexyl protons; 1.63, d, J 7 Hz, C9-H_3; 5.02, ddq, $J_{8,Me}$ 7 Hz, $J_{8,\beta-H2}$ 3.5 Hz, $J_{8,\beta-H6}$ 3.5 Hz, H8. trans-Allene (D7) decomposed before satisfactory CH analysis or M^+ could be obtained.

Elution with petroleum ether/ether (95:5) gave 2-α-methyl-4-α-t-butyl-1-β-(Z)-propenylcyclohexan-1-ol (D8) 15 mg). ν_{max} (liquid film) 3500, 1655, 710 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.87, d, J 6 Hz, C2-CH_3; 1.0-1.7, (s,m), 9H, (OH, cyclohexyl protons); 1.84, d, J 5 Hz, C9-H_3; 5.26, d, $J_{7,8}$ 12 Hz, H7; 5.47, dq, $J_{8,7}$ 12 Hz, $J_{8,Me}$ 5 Hz, H8 (Found: C, 80.50; H, 12.95. $C_{14}H_{26}O$ requires C, 79.94; H, 12.46).

Elution with petroleum ether/ether (93:7) gave 2-α-methyl-4-α-t-butyl-1-β-(E)-propenylcyclohexan-1-ol (D9) (D9) (14 mg), mp. 35-37°. ν_{max} (liquid film) 3525, 1670, 970 cm^{-1}. N.m.r. δ0.75, d, J 6 Hz, C2-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 1.0-1.6, (s,m), 9H, (OH, cyclohexyl protons); 1.68, d, J 5 Hz, C9-H_3; 5.35, d, $J_{7,8}$ 16 Hz, H7; 5.56, dq, $J_{8,7}$ 16 Hz, $J_{8,Me}$ 5 Hz, H8 (Found: C, 80.24; H, 12.67. $C_{14}H_{26}O$ requires C, 79.94; H, 12.46).

Further elution with petroleum/ether (93:7) gave the starting alkynol (B9) (292 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of alkynol (B9) (400 mg) with lithium aluminium hydride (80 mg) as above, but worked up with deuterium oxide, gave a crude product the components of which

were separated by chromatography on alumina.

trans-Allene (D7) (60 mg) identical (n.m.r.) with an authentic sample.

8-Deutero (Z)-alkenol (D8) (10 mg). N.m.r. δ 0.87, s, 9H, $C(CH_3)_3$; 0.95, d, J 6 Hz, C2-CH_3; 1.0-1.7, (s,m), 9H, (OH, cyclohexyl protons); 1.83, s, C9-H_3; 5.18, m, $W_{h/2}$ 4 Hz, H7.

8-Deutero (E)-alkenol (D9) (11 mg). N.m.r. δ0.75, d, J 6 Hz, C2-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 0.8-1.5, (s,m), 9H, (OH, cyclohexyl protons); 1.68, t, $J_{Me,D}$ 3 Hz, C9-CH_3; 5.35, m, H7.

Alkynol (B9) (293 mg) identical (n.m.r.) with an authentic sample.

Reaction of 2-α-methyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B9) with lithium aluminium hydride in tetrahydrofuran (refer to page 120).

The reaction mixture of alkynol (B9) (400 mg) and lithium aluminium hydride (80 mg) in tetrahydrofuran (20 ml) was heated under reflux for 48 h. Chromatography of the crude product on alumina gave trans-allene (D7) (124 mg) and (E)-alkenol (D9) (248 mg). Both were identical (n.m.r.) with authentic samples of (D7) and (D9) respectively.

Reaction of 2-α-methyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B9) with lithium aluminium deuteride in tetrahydrofuran (refer to page 120).

Reaction of alkynol (B9) (400 mg) with lithium aluminium deuteride (88.7 mg) as above gave a crude product

the components of which were separated by chromatography on alumina.

8-Deutero trans-allene (D7) (127 mg). N.m.r. δ 0.85, s, 9H, $C(CH_3)_3$; 0.92, d, J 6 Hz, C2-CH_3; 1.0-2.6, m, 8H, cyclohexyl protons; 1.62, s, C9-H_3.

7-Deutero and 8-deutero (E)-alkenols (D9) (255 mg) as a mixture (57:6). N.m.r. (7-deutero) δ 0.75, d, J 6 Hz, C2-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 0.8-1.6, (s,m), 9H, (OH, cyclohexyl protons); 1.67, d, J 6 Hz, C9-H_3; 5.55, m, H8. N.m.r. (8-deutero) as before.

Reaction of 2-α-methyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B9) with lithium aluminium deuteride in 2,5-dimethyl-tetrahydrofuran (refer to page 120).

The mixture of the alkynol (400 mg) and lithium aluminium deuteride (88.7 mg) was heated under reflux in 2,5-dimethyltetrahydrofuran (20 ml) and chromatography of the crude product on alumina gave:

8-Deutero trans-allene (D7) (300 mg) identical (n.m.r.) with an authentic sample.

7-Deutero (Z)-alkenol (D8) (28 mg). N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.9, d, J 6 Hz, C2-CH_3; 1.0-1.7, (s,m), 9H, (OH, cyclohexyl protons); 1.81, d, J 7 Hz, C9-H_3; 5.38, qt, $J_{8,Me}$ 7 Hz, $J_{8,D}$ 3 Hz, H8.

7-Deutero (E)-alkenol (D9) (23 mg) identical (n.m.r.) with an authentic sample.

Reaction of 2-α-methyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B12) with lithium aluminium hydride in diethyl ether (refer to page 120).

(a) The mixture of alkynol (B12) (500 mg) and lithium aluminium hydride (100 mg) in diethyl ether (25 ml) was heated under reflux for 96 h after which time the excess lithium aluminium hydride was destroyed with deuterium oxide. The crude product was adsorbed onto alumina (50 g).

Elution with petroleum ether/ether gave cis-allene (D10) (41 mg). ν_{max} (liquid film) 1970 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.93, d, J 5 Hz, C2-CH_3; 1.0-2.6, 8H, cyclohexyl protons; 1.59, d, J 7 Hz, C9-H_3; 4.98, m, H8. Sample decomposed before satisfactory CH analysis or M^+ could be obtained.

Elution with petroleum ether/ether (88:12) gave 8-deutero-2-α-methyl-4-α-t-butyl-1-α-(Z)-propenylcyclohexan-1-ol (D11) (11 mg). N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.86, d, J 5 Hz, C2-CH_3; 0.9-2.3, (s,m), 9H, (OH, cyclohexyl protons); 1.85, s, C9-H_3; 5.40, m, $W_{h/2}$ 6 Hz, H7.

Elution with petroleum ether/ether (86:14) gave 8-deutero-2-α-methyl-4-α-t-butyl-1-α-(E)-propenylcyclohexan-1-ol (D12) (11 mg). N.m.r. δ0.76, d, J 5 Hz, C2-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 0.9-2.4, (s,m), 9H, (OH, cyclohexyl protons); 1.72, s, C9-H_3; 5.65, m, $W_{h/2}$ 6 Hz, H7.

Further elution with petroleum ether/ether (86:14 and 50:50) gave the starting alkynol (B12) (420 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of the alkynol (B12) (500 mg) was carried out in the same manner as above, followed by chromatography of the crude product gave: cis-allene (D10) (30 mg); 8-deutero (Z)-alkenol (D11) (8 mg); 8-deutero (E)-alkenol (D12) (8 mg) and the starting compound (B12) (444 mg). The four products were identical (n.m.r.) with authentic samples of (D10), (D11), (D12) and (B12) respectively.

Reaction of 2-α-methyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B12) with lithium aluminium hydride in tetrahydrofuran (refer to page 120).

(a) The solution of alkynol (B12) (500 mg) and lithium aluminium hydride (100 mg) in tetrahydrofuran (25 ml) was heated under reflux for 48 h and chromatography of the crude product on alumina gave the following products:

cis-Allene (D10) (172 mg) identical (n.m.r.) with an authentic sample.

(Z)-Alkenol (D11) (8 mg). ν_{max} (liquid film) 3400-3500, 720 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.86, d, J 5 Hz, C2-CH_3; 0.9-2.3, (s,m), 9H, (OH, cyclohexyl protons); 1.87, d, J 6 Hz, C9-H_3; 5.2-5.7, ABq, 2H, vinylic protons (Found: M^+, 210.1979. Calc. for $C_{14}H_{26}O$: M^+, 210.1983).

(E)-Alkenol (D12) (259 mg), mp. 41-44. ν_{max} (liquid film) 3400, 1665, 970 cm^{-1}. N.m.r. δ0.76, d, J 5 Hz, C2-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 0.9-2.5, (s,m), 9H, (OH, cyclohexyl protons); 1.71, d, J 5 Hz, C9-H_3; 5.3-6.0, ABq, 2H, vinylic protons (Found: C, 80.38; H, 12.86. $C_{14}H_{26}O$ requires C, 79.94; H, 12.46).

Starting alkynol (B12) (9 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of the alkynol (B12) (500 mg) with lithium aluminium hydride (100 mg) as above, but the excess hydride was destroyed with deuterium oxide (3 ml), gave a crude product the components of which were separated by chromatography on alumina: cis-allene (D10) (198 mg) identical (n.m.r.) with an authentic sample. 8-Deutero (Z)-alkenol (D11) (9 mg) identical(n.m.r.) with an authentic sample. 7-Deutero and 8-deutero (E)-alkenols (D12) (248 mg) as a mixture (3:46).

Reaction of 2-α-methyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B12) with lithium aluminium hydride in 2,5-dimethyl-tetrahydrofuran (refer to page 120).

(a) A solution of the alkynol (400 mg) with lithium aluminium hydride (80 mg) in 2,5-dimethyltetrahydrofuran (20 ml) was heated under reflux for 6 h and the crude product was resolved into its components by chromatography on alumina: cis-Allene (D10) (267 mg); (Z)-alkenol (D11) (23 mg); (E)-alkenol (D12) (29 mg); starting alkynol (B12) (41 mg).

(b) Reaction of the alkynol (400 mg) as above, except the excess lithium aluminium hydride was destroyed by deuterium oxide (3 ml), gave a crude product the components of which were separated by chromatography on alumina: cis-Allene (D10) (259 mg); 8-deutero (Z)-alkenol (D11) (25 mg); 8-deutero (E)-alkenol (D12) (31 mg); starting alkynol (B12)

(51 mg). The four components were identical (n.m.r.) with authentic samples of (D10), (D11), (D12) and (B12) respectively.

N-Cyclohexyl-N-(2-methyl-4-t-butyl-1-cyclohexen-1-yl)amine (2.6)[28].

A solution of the mixture of ketones (2.2 and 2.3) (54.5 g) and cyclohexylamine (32.1 g) in benzene (271 ml) was boiled for 44 h in the presence of p-toluenesulfonic acid (0.4 g) with a Dean-Stark tube. Distillation at 102-110° (11 mm) gave the mixture of ketones (2.2 and 2.3) (1.4 g); at 112-124° (8-2.5 mm) gave a mixture of ketones and the amine (2.2, 2.3 and 2.6) (13.5 g). Pure amine (2.6) (48.8 g, 60% yield) boiled off at 122° (1 mm).

Condensation of N-cyclohexyl-N-(2-methyl-4-t-butyl-1-cyclohexen-1-yl)amine (2.6) with methyl iodide[28].

A solution of ethyl magnesium bromide (from 9.2 g of magnesium and 42.7 g of ethyl bromide) in anhydrous tetrahydrofuran (329 ml) was boiled with the amine (2.6) (48.8 g) for 18 h. After which time methyl iodide (27.8 g) was added dropwise and the reaction mixture was boiled for 30 h and poured into 10% hydrochloric acid (772 ml). The emulsion which formed was boiled for 3 h and extracted with ether (4 x 250 ml). The extract was washed with water, dried with magnesium sulphate, and distilled. A mixture of ketones, (2.2) and 2,6-dimethyl-4-t-butyl-1-cyclohexanone (15.4 g) was obtained, 84-88° (5-4 mm).

2,6-Dimethyl-4-t-butyl-1-cyclohexanone (2.7)[28].

To a suspension of sodium methoxide (from 4.2 g of sodium) in anhydrous benzene (56 ml), while cooling with ice, was added a mixture of the ketones (2.2 and 2.7) (15.4 g) and ethyl formate (10.3 g) in an atmosphere of nitrogen. The reaction mixture was stirred for 1 h while being cooled with ice, and kept at 5° for 40 h, poured into water and extracted with benzene (3 x 300 ml). The extract was washed with water and dried with magnesium sulphate. Distillation gave the ketone (2.7) (11 g), 80-90° (4 mm).

2,6-α,α-Dimethyl-4-α-t-butyl-1-β-propynyl- and 2,6-α,α-dimethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ols (B10 and B13).

2,6-Dimethyl ketone (2.7) (0.034 mol) in ether (40 ml) was added in small portions to the propynyllithium [prepared from propyne (0.15 mol) and n-butyllithium (0.05 mol) in ether (125 ml)] at -20°, and the resulting mixture was stirred for 45 h at room temperature. The whole reaction mixture was poured into saturated ammonium chloride solution (400 ml) and the crude product, isolated by means of ether, was adsorbed onto alumina (600 g).

Elution with petroleum ether/ether (93:7 and 92:8) gave alkynol (B10) (3.6 g, 48% yield), mp. 38-40°. ν_{max} (liquid film) 3500, 2100 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 1.03, d, J 6 Hz, 6H, C2- and C6-CH_3; 1.0-1.7, m, 7H, cyclohexyl protons; 1.17, s, OH; 1.82, s, C9-H_3 (Found: C, 81.07; H, 12,29. $C_{15}H_{26}O$ requires C, 81.08; H, 11.79).

Elution with petroleum ether/ether (85:15) gave alkynol (B13) (1.9 g, 25% yield) mp. 72-74°. ν_{max} (nujol mull) 3350, 2250 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.98, d, J 6 Hz, 6H, C2- and C6- CH_3; 1.0-1.7, m, 7H, cyclohexyl protons; 1.78, s, OH; 1.88, s, C9-H_3 (Found: C,81.22; H, 11.86. $C_{15}H_{26}O$ requires C, 81.08; H, 11.79).

Elution with petroleum ether/ether (80:20) gave an unidentified compound (0.4 g).

Reaction of 2,6-α,α-dimethyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B10) with lithium aluminium hydride in diethyl ether (refer to page 120).

The mixture of alkynol (B10) (500 mg) and lithium aluminium hydride (94.0 mg) in diethyl ether (25 ml) was heated under reflux for 96 h. After which time deuterium oxide (3 ml) was added and the crude product, isolated by means of ether, was adsorbed onto alumina (70 g).

Elution with petroleum ether gave trans-allene (D13) (70 mg). ν_{max} (liquid film) 1955 cm^{-1}. N.m.r. δ0.87, s, 9H, $C(CH_3)_3$; 0.95, d, J 6 Hz, 6H, C2- and C6-CH_3; 1.0-2.4, m, cyclohexyl protons; 1.64, d, J 7 Hz, C9-H_3; 5.10, ddq, $J_{8,Me}$ 7 Hz, $J_{8,2}$ 3.5 Hz, $J_{8,6}$ 3.5 Hz, H8. Sample decomposed before satisfactory CH analysis or M^+ could be obtained.

Elution with petroleum ether/ether (97:3) gave 8-deutero-2,6-α,α-dimethyl-4-α-t-butyl-1-β-(Z)-propenylcyclohexan-1-ol (D14) (5 mg). N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.87, d, J 6 Hz, 6H, C2- and C6-CH_3; 0.5-1.6, (s,m), 8H, (OH, cyclohexyl protons); 1.82, s, C9-H_3; 4.98, m, $W_{h/2}$ 6 Hz, H7 (Found: M^+ 225.2198. Calc. for $C_{15}H_{27}DO$: M^+,

225.2202).

Further elution with petroleum ether/ether (97:3) gave 8-deutero-2,6-α,α-dimethyl-4-α-t-butyl-1-β-(E)-propenylcyclohexan-1-ol (D15) (6 mg). N.m.r. δ0.77, d, J 6 Hz, 6H, C2- and C6-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 0.9-1.6, (s,m), 8H, (OH, cyclohexyl protons); 1.70, s, C9-H_3; 5.15, m, $W_{h/2}$ 6 Hz, H7.

Finally, elution with petroleum ether/ether (96:4) gave the starting alkynol (B10) (401 mg) identical (n.m.r.) with an authentic sample.

Reaction of 2,6-α,α-dimethyl-4-α-t-butyl-1-β-propynylcyclohexan-1-ol (B10) with lithium aluminium hydride in tetrahydrofuran (refer to page 120).

(a) The mixture of the alkynol (400 mg) and lithium aluminium hydride (75.2 mg) in tetrahydrofuran (20 ml) was heated under reflux for 48 h and chromatography of the crude product on alumina gave the following products:

trans-Allene (D13) (118 mg) identical (n.m.r.) with an authentic sample.

(E)-Alkenol (D15) (248 mg). ν_{max} (liquid film) 3525, 970 cm^{-1}. N.m.r. δ0.78, d, J 6 Hz, 6H, C2- and C6-CH_3; 0.87, s, 9H, $C(CH_3)_3$; 0.9-1.6, (s,m), 8H, (OH, cyclohexyl protons); 1.72, d, J 6 Hz, C9-H_3; 5.18, d, $J_{7,8}$ 16 Hz, H7; 5.52, dq, $J_{8,7}$ 16 Hz, $J_{8,Me}$ 6 Hz, H8 (Found: C, 80.69; H, 12.84. $C_{15}H_{28}O$ requires C, 80.29; H, 12.58).

An unidentified compound (13 mg).

(b) Reaction of the alkynol (810) (400 mg) as above, except the excess lithium aluminium hydride was destroyed by deuterium oxide (3 ml), followed by chromatography of the crude product gave: trans-allene (D13) (112 mg) identical (n.m.r.) with an authentic sample; 7-deutero and 8-deutero (E)-alkenols (D15) (249 mg) as a mixture (3:58); and an unidentified product (8 mg).

Reaction of 2,6-α,α-dimethyl-4-α-t-butyl-1-butyl-1-β-propynylcyclohexan-1-ol with lithium aluminium hydride in 2,5-dimethyltetrahydrofuran (refer to page 120).

(a) The mixture of the alkynol (400 mg) and lithium aluminium hydride (75.2 mg) in 2,5-dimethyltetrahydrofuran (20 ml) was heated under reflux for 6 h. Chromatography of the crude product on alumina gave the following products.

trans-Allene (D13) (328 mg) identical (n.m.r.) with an authentic sample.

(Z)-Alkenol (D14) (9 mg). ν_{max} (liquid film) 3300-3500, 715 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 0.87, d, J 6 Hz, 6H, C2- and C6-CH_3; 0.5-1.6, (s,m), 8H, (OH, cyclohexyl protons); 1.82, d, J 6 Hz, C9-H_3; 4.99, d, J 12 Hz, H7; 5.46, dq, $J_{8,7}$ 12 Hz, $J_{8,Me}$ 6 hz, H8 (Found: M^+ 224.2142. Calc. for $C_{15}H_{28}O$: M^+, 224.2140).

(E)-Alkenol (D15) (18 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of the alkynol (B10) (400 mg) with lithium aluminium hydride (75.2 mg) as above, except that deuterium oxide (3 ml) was used to quench the reaction,

gave a crude product the components of which were separated by chromatography on alumina: trans-allene (D13) (331 mg); 8-deutero (Z)-alkenol (D14) (8 mg); 8-deutero (E)-alkenol (D15) (16 mg); each of which was identical (n.m.r.) with an authentic sample.

Reaction of 2,6-α,α-dimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B13) with lithium aluminium hydride in diethyl ether (refer to page 120).

The mixture of the alkynol (300 mg) and lithium aluminium hydride (56.4 mg) in diethyl ether (15 ml) was heated under reflux for 96 h. After which time deuterium oxide (3 ml) was added to quench the reaction and chromatography of the crude product on alumina gave:

cis-Allene (D16) (10 mg). ν_{max} (liquid film) 1970 cm^{-1}. N.m.r. δ0.87, s, 9H, $C(CH_3)_3$; 0.94, d, J 7 Hz, 6H, C2- and C6-CH_3; 0.6-2.4, m, 7H, cyclohexyl protons; 1.63, d, J 7 Hz, C9-H_3; 5.10, ddq, $J_{8,Me}$ 7 Hz, $J_{8,2}$ 3.5 Hz, $J_{8,6}$ 3.5 Hz, H8. Sample decomposed before satisfactory CH analysis or M^+ could be obtained.

Alkynol (B13) (288 mg) identical (n.m.r.) with an authentic sample.

Reaction of 2,6-α,α-dimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B13) with lithium aluminium hydride in 2,5-dimethyltetrahydrofuran (refer to page 120).

(a) The solution of the alkynol (300 mg) and lithium aluminium hydride (56.4 mg) in 2,5-dimethyltetrahydrofuran (15 ml) was heated under reflux for 6 h and the crude product,

isolated by means of ether, was adsorbed onto alumina (30 g).

Elution with petroleum ether gave the cis-allene (D16) (235 mg) identical (n.m.r.) with an authentic sample.

Elution with petroleum ether/ether (90:10) gave 2,6-α,α-dimethyl-4-α-t-butyl-1-α-(Z)-propenylcyclohexan-1-ol (D17) (6 mg). ν_{max} (liquid film) 3300-3500, 725 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.90, α, J 6 Hz, 6H, C2- and C6-CH_3; 1.0-2.0, (s,m), 8H, (OH, cyclohexyl protons); 1.87, d, J 7 Hz, C9-H_3; 5.16, d, $J_{7,8}$ 12 Hz, H7; 5.62, dq, $J_{8,7}$ 12 Hz, $J_{8,Me}$ 7 Hz, H8 (Found: M^+, 224.2131. Calc. for $C_{15}H_{28}O$: M^+, 224.2140).

Elution with petroleum ether/ether (80:20) gave 2,6-α,α-dimethyl-4-α-t-butyl-1-α-(E)-propenylcyclohexan-1-ol (8 mg). ν_{max} (nujol mull) 3475, 1665, 970 cm^{-1}. N.m.r. δ0.75, d, J 6 Hz, 6H, C2- and C6-CH_3; 0.87, s, 9H, $C(CH_3)_3$; 0.8-1.7, (s,m), 8H, (OH, cyclohexyl protons); 1.74, d, J 5 Hz, C9-H_3; 5.40, d, $J_{7,8}$ 15 Hz, H7; 5.63, dq, $J_{8,7}$ 15 Hz, $J_{8,Me}$ 5 Hz, H8 (Found: C, 79.96; H, 12.65. $C_{15}H_{28}O$ requires C, 80.29; H, 12.58).

Further elution with petroleum ether/ether (80:20) gave the starting alkynol (B13) (21 mg) identical (n.m.r.) with an authentic sample.

(b) Reaction of the alkynol (300 mg) with lithium aluminium hydride (56.4 mg) as above, except that deuterium oxide was added to quench the reaction, gave a crude product the components of which were separated by chromatography on alumina.

cis-Allene (D16) (222 mg) identical (n.m.r.) with an authentic sample.

8-Deutero (Z)-alkenol (D17) (8 mg). N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.90, d, J 6 Hz, 6H, C2- and C6-CH_3; 1.0-2.0, (s,m) 8H, (OH, cyclohexyl protons); 1.87, s, C9-H_3; 5.20, s, H7.

8-Deutero (E)-alkenol (D18) (11 mg). N.m.r. δ0.77, d, J 6 Hz, 6H, C2- and C6-CH_3; 0.87, s, 9H, $C(CH_3)_3$; 0.8-1.7, (s,m), 8H, (OH, cyclohexyl protons); 1.75, s, C9-H_3; 5.42, m, $W_{h/2}$ 6 Hz, H7.

Alkynol (B13) (27 mg) identical (n.m.r.) with an authentic sample.

Reaction of 2,6-α,α-dimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B13) with lithium aluminium hydride in tetrahydrofuran (refer to page 120).

(a) the mixture of alkynol (B13) (300 mg) and lithium aluminium hydride (56.4) in tetrahydrofuran (15 ml) was heated under reflux for 48 h and chromatography of the crude product on alumina gave the cis-allene (D16) (133 mg) and the (E)-alkenol (D18) (132 mg), mp. 50-52°. The two compounds were identical (n.m.r.) with authentic samples of (D16) and (D18) respectively.

(b) Reaction of the alkynol (300 mg) with lithium aluminium hydride (56.4 mg) as above, except that deuterium oxide (3 ml) was added to quench the reaction, gave a crude product the components of which were separated by chromatography on alumina: cis-allene (D16) (143 mg) identical

(n.m.r.) with an authentic sample; 7-deutero and 8-deutero (E)-alkenols (D18) (133 mg) as a mixture (3:41).

Ethyl 2,6,6-trimethyl-4-t-butyl-1-cyclohexanone-2-carboxylate (2.8)[28]

To a suspension of sodium hydride (1 mol) in anhydrous benzene (175 ml), while cooling with ice, was added ethyl 4-t-butyl-1-cyclohexanone-2-carboxylate (2.1) (0.2 mol) over 20 min. and then methyl iodide (0.58 mol) after evolution of hydrogen had moderated. The reaction mixture was stirred and cooled for 1 h, boiled for 4 h, and cooled. To the reaction mass a further lot of methyl iodide (0.86 mol) was added, and the resulting mixture was boiled for 36 h. To the reaction mixture, cooled with ice, ethanol (15 ml) was added cautiously and then water (25 ml). The mixture was stirred for 15 min and poured into water (485 ml). The aqueous solution, which was separated from the benzene solution, was extracted with ether (3 x 150 ml). The extract together with the benzene solution was washed with water, dried with magnesium sulphate, and spinning-band distilled. Two fractions were obtained. The first fraction (5.8 g) consisted of a mixture of keto ester (2.8) and (2,2,6-trimethyl- and 2,2,6,6-tetramethyl-) 4-t-butyl-1-cyclohexanones; bp. 70-90^{o} (0.5 mm). The second fraction consisted of the keto ester (2.8) (21.1 g, 39% yield based on mole of keto ester (2.1)]; bp. 80-100^{o} (0.5 mm).

2,2,6-Trimethyl-4-t-butyl-1-cyclohexanone (2.9)[28]

The mixture of keto ester (2.8) (0.078 mol) and p-toluenesulfonic acid monohydrate (7 g) and boiled for 72 h with 50% acetic acid (56 ml) containing concentrated sulfuric acid (7 ml). The reaction mixture was poured into water (250 ml) and extracted with hexane (2 x 250 ml). The extract was washed with 20% aqueous sodium hydroxide solution and with water, dried with magnesium sulphate, and distilled. Distillation at 105-110° (17 mm) gave the ketone (2.9) [11.9 g, 77% yield, calculated on the keto ester (2.8)].

2,2,(6-α)-Trimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B14)

A solution of the ketone (2.9) (0.1 mol) in ether (80 ml) was added to a solution of propynylmagnesium bromide [prepared as before from magnesium (4 g), ethyl bromide (14 ml) and propyne (30 ml)] in ether (160 ml) and the resulting mixture was stirred for 20 h at room temperature. After which time it was poured into saturated ammonium chloride solution (300 ml). The crude product was extracted with ether (2 x 200 ml), and adsorbed onto alumina (700 g).

Elution with petroleum ether/ether (99:1) gave a mixture of the alkynol (B14) and 2 other compounds, (9.3 g).

Further elution with petroleum ether/ether (99:1 and 98:2) gave the pure alkynol (B14) (6.8 g), mp. 48-50°. ν_{max} (nujol mull) 3520, 2250 cm^{-1}. N.m.r. δ0.82, s, 9H, $C(CH_3)_3$; 0.97, s, C2-β-CH_3; 1.0, d, J 6 Hz, C6-CH_3; 1.08, s, C2-α-CH_3; 1.1-1.6, m, 6H, cyclohexyl protons; 1.72, s, OH; 1.85, s, C9-H_3 (Found: C, 81.45; H, 12.10. $C_{16}H_{28}O$

requires C, 81.29; H, 11.95).

Elution with petroleum ether/ether (50:50) gave a mixture of the alkynol (B14) and two other compounds, (8.4 g).

Reaction of 2,2,(6-α)-trimethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ol (B14) with lithium aluminium hydride in tetrahydrofuran (refer to page 120).

The mixture of alkynol (400 mg) and lithium aluminium hydride (70.8 mg) in tetrahydrofuran (20 ml) was heated under reflux for 48 h. The crude product, isolated by means of ether, was adsorbed onto alumina (50 g).

Elution with petroleum ether gave cis-allene (D19) (253 mg). ν_{max} (liquid film) 1965 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; obs., C6-CH_3; 0.98, s, C2-β-CH_3; 1.05, s, C2-α-CH_3; 0.6-2.5, m, 6H, cyclohexyl protons; 1.62, d, J 6 Hz, C9-H_3; 5.08, dq, $J_{8,Me}$ 6 Hz, $J_{8,6}$ 3.5 Hz, H8 (Found: C, 86.99; H, 13.00. $C_{16}H_{28}$ requires C, 87.19; H, 12.81).

Elution with petroleum ether/ether (80:20) gave 2,2,(6-α)-trimethyl-4-α-t-butyl-1-α-(E)-propenylcyclohexan-1-ol (D21) (94 mg). ν_{max} (liquid film) 3510, 1665, 970 cm^{-1}. N.m.r. δ0.70, d, J 6 Hz, C6-CH_3; 0.75, s, C2-β-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 0.98, s, C2-α-CH_3; 1.0-2.0, (s,m), 7H, (OH, cyclohexyl protons); 1.74, d, J 5 Hz, C9-H_3; 5.4-5.8, ABq, 2H, vinylic protons (Found: C, 80.41; H, 12.49. $C_{16}H_{30}O$ requires C, 80.60; H, 12.70).

Reaction of 2,2,(6-α)-trimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B14) with lithium aluminium deuteride in tetrahydrofuran (refer to page 120).

Reaction of the alkynol (400 mg) with lithium aluminium deuteride (78 mg) in tetrahydrofuran (20 ml) as above gave a crude product the components of which were separated by chromatography on alumina.

8-Deutero cis-allene (D19) (247 mg). N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; obs., C6-CH_3; 0.98, s, C2-β-CH_3; 1.05, s, C2-α-CH_3; 0.6-2.5, m, 6H, cyclohexyl protons; 1.62, s, C9-H_3.

7-Deutero (E)-alkenol (D21) (108 mg). N.m.r. δ0.70, d, J 6 Hz, C6-CH_3; 0.75, s, C2-β-CH_3; 0.85, s, 9H, $C(CH_3)_3$; 0.97, s, C2-α-CH_3; 1.0-2.0, (s,m), 7H, (OH, cyclohexyl protons); 1.74, d, J 7 Hz, C9-H_3; 5.62, m, H8.

Reaction of 2,2,(6-α)-trimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B14) with lithium aluminium hydride in 2,5,-dimethyltetrahydrofuran (refer to page 120).

The mixture of the alkynol (500 mg) and lithium aluminium hydride (88.5 mg) in 2,5-dimethyltetrahydrofuran (25 ml) was heated under reflux for 6 h, followed by chromatography of the crude product on alumina gave the cis-allene (D19) (421 mg) and the (E)-alkenol (D21) (10 mg), identical (n.m.r.) with authentic samples of (D19) and (D21) respectively.

Reaction of 2,2,(6-α)-trimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B14) with lithium aluminium deuteride in 2,5-dimethyltetrahydrofuran (refer to page 120).

The mixture of the alkynol (300 mg) and lithium aluminium deuteride (58.5 mg) was heated under reflux for 8 h, followed by chromatography of the crude product on alumina gave the 8-deutero cis-allene (D19) (254 mg) and the 7-deutero (E)-alkenol (D21) (10 mg), identical (n.m.r.) with authentic samples of (D19) and (D21) respectively.

Reaction of 2,2,(6-α)-trimethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B14) with lithium aluminium deuteride in diethyl ether (refer to page 120).

The mixture of the alkynol (400 mg) and lithium aluminium deuteride (78 mg) in diethyl ether (20 ml) was heated under reflux for 96 h and chromatography of the crude product on alumina gave 8-deutero cis-allene (D19) (37 mg) and alkynol (B14) (360 mg), identical (n.m.r) with the authentic samples of (D19) and (B14) respectively.

2,2,6,6-Tetramethyl-4-t-butyl-1-cyclohexanone (2.10).

To a suspension of the sodium hydride (0.55 mol), cooled with ice, was added dropwise the 2,2,6-trimethyl ketone (2.9) (0.11 mol) over 30 min. Methyl iodide (0.22 mol) was then added and the mixture was stirred and cooled for 1 h. The reaction mass was boiled for 20 h. Ethanol (25 ml) was added dropwise while cooling with ice, followed by water (25 ml). The whole mixture was poured into water (300 ml) and extracted with ether

(2 x 150 ml). Crystallisation of the crude product from ethanol/water gave crystalline 2,2,6,6-tetramethyl ketone (2.10) [4.1 g, 18% yield calculated on ketone (2.9)]. The residual (6.2 g) consisted of a mixture of ketones (2.9 and 2.10).

2,2,6,6-Tetramethyl-4-α-t-butyl-1-α-propynylcyclohexan-1-ol (B15).

(a) To the propynyllithium [prepared from propyne (0.12 mol) and n-butyllithium (0.04 mol) in ether (50 ml)] was added the solution of a mixture of ketones (2.9 and 2.10) (2.6 g) in ether (30 ml) at -20° and the resulting mixture was stirred for 39 h at room temperature. After which time the reaction mass was poured into saturated ammonium chloride solution (50 ml) and the crude product isolated by means of ether, was adsorbed onto alumina (300 g).

Elution with petroleum ether/ether (97:3) gave a compound (74 mg) which was not identified.

Elution with petroleum ether/ether (96:4) gave alkynol (B15) (2.2 g), mp. 50-52°. ν_{max} (nujol mull) 3600, 2200 cm^{-1}. N.m.r. δ0.85, s, 9H, $C(CH_3)_3$; 1.05, s, 6H, C2-β- and C6-β-CH_3; 1.13, s, 6H, C2-α- and C6-α-CH_3; 1.18, s, 5H, cyclohexyl protons; 1.67, s, OH; 1.83, s, C9-H_3 (Found: C, 81.32; H, 11.81. $C_{17}H_{30}O$ requires C, 81.46; H, 12.08).

Elution with petroleum ether/ether (96:4 and 94:6) gave alkynol (B14) (720 mg) identical (n.m.r.) with an authentic sample.

(b) A solution of the tetramethyl ketone (2.10) (3.2 g) in ether (40 ml) was added dropwise to the propynyl-magnesium bromide solution in ether (25 ml) [prepared from magnesium (0.7 g), ethyl bromide (3 ml), and propyne(5 ml)], and the resulting mixture was stirred for 18 h at room temperature. It was then poured into saturated ammonium chloride solution (50 ml) and extracted with ether (3 x 50 ml). The crude product (3.4 g) was adsorbed onto alumina (350 g).

Elution with petroleum ether gave a mixture of three products (1.0 g) which composed of the alkynol (B15), 2,2,6,6-tetramethyl-4-α-t-butylcyclohexan-1-α-ol (B16) and an unidentified component. Further elution gave a mixture of alkynol (B15) and the alcohol (B16) (1.62 g), from which a portion (394 mg) was recrystallized from petroleum ether and gave the pure secondary alcohol (B16) (60 mg), mp. 105-107.5°. ν_{max} (nujol mull) 3550 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.87, s, 6H, C2- and C6- β-CH_3; 0.93, s, 6H, C2- and C6-α-CH_3; 0.9-1.9, (s,m), 6H, (OH, cyclohexyl protons); 2.83, s, H1 (Found: C, 79.07; H, 13.37. $C_{14}H_{28}O$ requires C, 79.16; H, 13.30). Final elution with petroleum ether and petroleum ether/ether (50:50) gave a mixture of the secondary alcohol (B16) and an unidentified component (290 mg).

Reaction of 2,2,6,6-tetramethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ol with lithium aluminium hydride in tetra-hydrofuran (refer to page 120).

The solution of alkynol (B15) (400 mg) in tetra-

hydrofuran (20 ml) was heated under reflux with lithium aluminium hydride (67 mg) for 48 h, and the crude product, isolated by means of ether, was adsorbed onto alumina (50 g).

Elution with petroleum ether gave cis-allene (D22) (91 mg). ν_{max} (liquid film) 1947 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 1.02, s, 6H, C2-β- and C6-β-CH_3; 1.13, s, 6H, C2-α- and C6-α-CH_3; 0.9-1.7, m, 5H, cyclohexyl protons; 1.61, d, J 7 Hz, C9-H_3; 5.13, q, J 7 Hz, H8. Sample decomposed before satisfactory CH analysis or M^+ could be obtained.

Elution with petroleum ether/ether (97:3) gave 2,2,6,6-tetramethyl-4-α-t-butyl-1-α-(E)-propenylcyclohexan-1-ol (D24) (22 mg). ν_{max} (liquid film) 3450-3550, 978 cm^{-1}. N.m.r. δ0.73, s, 6H, C2-β- and C6-β-CH_3; 0.87, s, 9H, $C(CH_3)_3$; 1.07, s, 6H, C2-α- and C6-α-CH_3; 1.27, s, 5H, cyclohexyl protons; 1.52, s, OH; 1.72, d, J 6 Hz, C9-H_3; 5.2-5.8, ABq, 2H, vinylic protons.

Finally, elution with petroleum ether/ether (50:50) gave 2,2,6,6-tetramethyl-4-α-t-butylcyclohexan-1-α-ol (B16) (233 mg), identical with an authentic sample.

Reaction of 2,2,6,6-tetramethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ol with lithium aluminium deuteride in tetrahydrofuran (refer to page 120).

Reaction of the alkynol (400 mg) with lithium aluminium deuteride (73.6 mg) as above gave a crude product the components of which were separated by chromatography on alumina.

8-Deutero cis-allene (D22) (93 mg). ν_{max} (liquid

film) 1950 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 1.00, s, 6H, C2-β- and C6-β-CH_3; 1.13, s, 6H, C2-α- and C6-α-CH_3; 0.9-1.7, m, 5H, cyclohexyl protons; 1.60, s, C9-H_3.

7-Deutero (E)-alkenol (D24) (9 mg). N.m.r. δ0.73, s, 6H, C2-β- and C6-β-CH_3; 0.87, s, 9H, $C(CH_3)_3$; 1.08, s, 6H, C2-α- and C6-α-CH_3; 1.30, s, 5H, cyclohexyl protons; 1.45, s, OH; 1.73, d, J 6 Hz, C9-H_3; 5.5, m, H8.

1-Deutero alcohol (B16) (234 mg). N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.87, s, 6H, C2-β- and C6-β-CH_3; 0.93, s, 6H, C2-α- and C6-α-CH_3; 1.0-1.6, (s,m), 6H, (OH, cyclohexyl protons).

Reaction of 2,2,6,6-tetramethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ol (B15) with lithium aluminium hydride in 2,5-dimethyltetrayhdrofuran (refer to page 120).

A solution of the alkynol (100 mg) in 2,5-dimethyl-tetrahydrofuran (5 ml) was heated under reflux with lithium aluminium hydride (16.7 mg) for 8 h, followed by chromatography of the crude product on alumina gave: cis-allene (D22) (80 mg); secondary alcohol (B16) (12 mg); each of which was identical (n.m.r.) with an authentic sample.

Reaction of 2,2,6,6-tetramethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ol (B15) with lithium aluminium deuteride in 2,5-dimethyltetrahydrofuran (refer to page 120).

Reaction of the alkynol (200 mg) with lithium aluminium deuteride (36.8 mg) as above, followed by chromatography of the crude product on alumina gave the 8-deutero cis-allene (D22) (160 mg) and the 1-deutero

secondary alcohol (B16) (25 mg); identical (n.m.r.) with authentic samples of (D22) and (B16) respectively.

Reaction of 2,2,6,6-tetramethyl-4-α-t-butyl-1-α-propynyl-cyclohexan-1-ol (B15) with lithium aluminium deuteride in diethyl ether (refer to page 120).

(a) A solution of the alkynol (200 mg) in diethyl ether (10 ml) was heated under reflux with lithium aluminium deuteride (37 mg) for 96 h. Chromatography of the crude product on alumina gave 8-deutero cis-allene (D22) (42 mg) and the starting alkynol (B15) (155 mg); identical (n.m.r.) with authentic samples of (D22) and (B15) respectively.

(b) Reaction of the alkynol (B15) was repeated exactly as above and gave 8-deutero cis-allene (D22) (39 mg) and the starting compound (B15) (157 mg).

Reduction of 2,2,6-trimethyl-4-t-butylcyclohexanone (2.9) and 2,2,6,6-tetramethyl-4-t-butylcyclohexanone (2.10) with lithium aluminium hydride in diethyl ether (refer to page 120).

A solution of a mixture of the ketones (2.9 and 2.10) (250 mg) in diethyl ether (17 ml) was heated under reflux for 7 h with lithium aluminium hydride (45 mg). The crude product, isolated by means of ether, was adsorbed onto alumina (50 g).

Elution with petroleum ether/ether (98:2) gave the secondary alcohol (B16) (154 mg) identical (n.m.r.) with

an authentic sample.

Elution with petroleum ether/ether (95:5) gave the 2,2,6-trimethyl-4-α-t-butylcyclohexan-1-β-ol (B17) (67 mg), mp. 67-69°. ν_{max} (nujol mull) 3350 cm^{-1}. N.m.r. δ0.83, s, 9H, $C(CH_3)_3$; 0.87, s, 3H, C2-β-CH_3; 0.98, s, 3H, C2-α-CH_3; 0.98, s, J 6 Hz, C6-CH_3; 1.0-2.2, (s,m), 7H, (OH, cyclohexyl protons); 2.78, d, J 10 Hz, H1.

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TABLE 1

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B7) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

% Reaction	Solvent	Temp(°C),time(h))	Yield (%)		Attack by H^- (D^-) at C4:C5	
			allene(C4)	(E)-alkenol(C3)	leading to (C3)	overall
90	Et_2O	35,16	69	26	23:3	23:72
93	Et_2O	35,16	65	32	27:5	27:70
92	Et_2O	35,16	68	32	-	-
99	THF	35,16	28	71	30:41	30:69
94	THF	35,16	24	75	26:49	26:73
97	THF	35,16	24	73	-	-
100	THF	65,2.5	55	40	24:16	24:71
100	THF	65,2.5	59	35	20:15	20:74
100	THF	65,2.5	58	37	-	-
100	2,5-Me_2-THF	35,16	51	42	25:17	25:69
92	2,5-Me_2-THF	65,2.5	67	30	23:7	23:74
98	2,5-Me_2-THF	91,0.5	75	25	25:0	25:75
34	Benzene	80,1	73	21	-	-
35	Benzene	80,4	68	26	7:19	7:87
70	Benzene	80,20	83	18	-	-

TABLE 2 and TABLE 3

(2)-PRODUCT YEILDS OF REACTIONS OF ALKYNOL (B5) WITH LITHIUM ALUMINIUM DEUTERIDE

		Yield (%)		Attack by D^- at C4:C5	
Solvent	Temp.(°C),time(h)	Allene(C1)	(E)-alkenol(C2)	leading to (C2)	overall
Et_2O	35,89	84	trace	-	Ca.0:84
THF	35,89	30	60	60:0	60:30
THF	65,2.5	66	18	18:0	18:66
2,5-Me_2-THF	65,2.5	92	2	2:0	2:92

(3)-PRODUCT YEILDS OF REACTIONS OF ALKYNOL (B6) WITH LITHIUM ALUMINIUM DEUTERIDE

		Yield (%)			Attack by D^- at C3:C4	
Solvent	Temp.(°C),time(h)	Allene(C9)	(Z)-alkenol(C11)	(E)-alkenol(C10)	Leading to (C10)	Overall
Et_2O	35,44	51	12	36	36:0	48:51
THF	35,44	-	-	79	79:0	79:0

TABLE 4

PRODUCT YIELDS OF REACTIONS OF ALKYNOL(B4) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

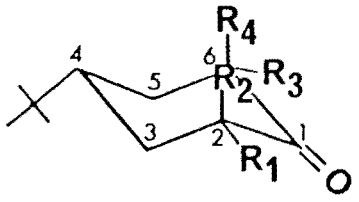
% Reaction	Solvent	Temp.(°C), time(h)	Yield (%)				Attack by H^- (D^-) at C4:C5	
			Allene(C5)	Cyclopropane derivative(C8)	Dimer(C7)	(E)-alkenol(C6)	leading to (C6)	overall
67	Et_2O	35,2.75	10	-	-	78	-	-
74	Et_2O	35,2.75	10	-	-	73	48:25	48:35
57	THF	20,1	-	-	-	67	-	-
100	THF	20,3	-	-	-	80	53:27	53:27
100	THF	65,4	-	9	20	54	-	-
100	THF	65,17	-	4	22	48	48:0	48:26
100	THF	65,4	-	7	30	51	46:5	46:42[a]
100	THF	65,4	8	6	8	67	47:20	47:42[a,b]

[a] Reference 34

[b] THF used was 10 times the normal volume.

TABLE 5

REDUCTION OF SUBSTITUTED 4-t-BUTYLCYCLOHEXANONES AND THE CHEMICAL SHIFTS (^{1}H and ^{13}C N.M.R.) OF THE RESULTING PROPARGYL ALCOHOLS.



R_1	R_2	R_3	R_4	relative yield, %[a,b]		^{1}H n.m.r. OH (ppm)[c]		^{13}C n.m.r. C-1 (ppm)	
				Ax. OH	Eq. OH	Ax. OH	Eq. OH	Ax. OH	Eq. OH
H	H	H	H	17	83	1.27	1.90	65.91	69.72
CH_3	H	H	H	40	60	1.27	1.80	69.03	73.44
CH_3	H	CH_3	H	65	35	1.17	1.78	72.30	77.24
CH_3	CH_3	CH_3	H	0	100	-	1.72	-	78.62
CH_3	CH_3	CH_3	CH_3	0	100	-	1.67	-	79.19

[a]Normalized, % axial alcohol + % equatorial alcohol = 100%.

[b]Ax. = axial and Eq. = equatorial. [c]Spectra were obtained in about the same concentration scale.

TABLE 6

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B8) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

% Reaction	Solvent	Temp.(°C),time(h)	Yield (%)			Attack by H^- (D^-) at C7:C8	
			allene(D1)	(Z)-alkenol(D2)	(E)-alkenol(D3)	leading to (D3)	overall
92	THF	65,5	20	-	71	-	-
88	THF	65,5	20	-	70	53:17	53:37
86	2,5-Me_2-THF	65,5.5	31	9	48	-	-
88	2,5-Me_2-THF	65,5.5	32	8	47	8:39	16:71
97	2,5-Me_2-THF	91,1	65	4	17	-	-
94	2,5-Me_2-THF	91,1	74	4	13	7.6	11.80
17	Et_2O	35,24	37	15	37	-	-
53	Et_2O	35,96	59	6	24	-	-
30	Et_2O	35,96	61	6	26	16:10	22:71

TABLE 7

PRODUCT YEIDLS OF REACTIONS OF ALKYNOL (B9) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

% Reaction	Solvent	Temp.(°C),time(h)	Yield (%)			Attack by H^- (D^-) at C7:C8	
			allene(D7)	(Z)-alkenol(D8)	(E)-alkenol(D9)	leading to (D9)	overall
100	THF	65,48	34	-	61	-	-
100	THF	65,48	34	-	63	57:6	57:40
100	2,5-Me_2-THF	91,6	81	7	6	6:0	13:81
27	Et_2O	35,97	66	14	13	-	-
27	Et_2O	35,97	61	9	10	10:0	19:61

TABLE 8

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B10) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

			Yield (%)			Attack by H^-(D^-) at C7:C8	
% Reaction	Solvent	Temp.(°C), time(h)	allene(D13)	(Z)-alkenol(D14)	(E)-alkenol(D15)	leading to (D15)	overall
100	THF	65,48	32	-	61	-	-
100	THF	65,48	30	-	61	58:3	58:33
100	2,5-Me_2-THF	91,6	88	2	5	-	-
100	2,5-Me_2-THF	91,6	89	2	4	4:0	6:89
20	Et_2O	35,96	76	5	6	6:0	11:76

TABLE 9

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B11) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

			Yield (%)			Attack by H^-(D^-) at C7:C8	
% Reaction	Solvent	Temp.(°C),time(h)	allene(D4)	(Z)-alkenol(D5)	(E)-alkenol(D6)	leading to (D6)	overall
100	THF	65,23	18	4	69	-	-
100	THF	65,23	15	4	75	75:0	79:15
100	2,5-Me_2-THF	91,10	34	3	54	-	-
100	2,5-Me_2-THF	91,10	36	2	48	48:0	50:36
65	Et_2O	35,23	6	5	83	-	-
59	Et_2O	35,45	8	4	84	84:0	88:8
77	Et_2O	35,45	8	5	84	-	-
88	Et_2O	35,96	9	8	80	-	-
91	Et_2O	35,96	8	7	79	79:0	86:8
93	Et_2O	35,96	8	9	77	77:0	86:8

TABLE 10

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B12) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

			Yield (%)			Attack by H^-(D^-) at C7:C8	
% Reaction	Solvent	Temp.(°C),time(h)	allene(D10)	(Z)-alkenol(D11)	(E)-alkenol(D12)	leading to (D12)	overall
100	THF	65,48	43	2	49	46:3	48:46
98	THF	65,48	38	2	52	-	-
90	2,5-Me_2-THF	91,6	81	6	8	-	-
87	2,5-Me_2-THF	91,6	80	7	9	9:0	16:80
11	Et_2O	35,96	58	14	14	14:0	28:58
16	Et_2O	35,96	56	14	14	14:0	28:56

TABLE 11

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B13) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

% Reaction	Solvent	Temp.(°C),time (h)	Yield (%)			Attack by H^-(D^-) at C7:C8	
			allene(D16)	(Z)-alkenol(D17)	(E)-alkenol(D18)	leading to (D18)	overall
100	THF	65,48	48	-	44	-	-
100	THF	65,48	51	-	44	41:3	41:54
93	2,5-Me_2-THF	91,6	91	2	3	-	-
91	2,5-Me_2-THF	91,6	88	3	4	4:0	7:88
4	Et_2O	35,96	90	-	-	-	0:90

TABLE 12

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B14) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

% Reaction	Solvent	Temp.(°C),time (h)	Yield (%)			Attack by $H^-(D^-)$ at C7:C8	
			allene(D19)	(Z)-alkenol(D20)	(E)-alkenol(D21)	leading to (D21)	overall
100	THF	65,48	68	-	23	-	-
100	THF	65,48	66	-	27	27:0	27:66
100	2,5-Me_2-THF	91,6	90	-	2	-	-
100	2,5-Me_2-THF	91,8	91	-	3	3:0	3:91
10	Et_2O	35,96	99	-	-	-	0:99

TABLE 13

PRODUCT YIELDS OF REACTIONS OF ALKYNOL (B15) WITH LITHIUM ALUMINIUM HYDRIDE (DEUTERIDE)

% Reaction	Solvent, temp.(°C),time(h)	Yield (%)				Attack by H^- (D^-) at C7:C8	
		Allene (D22)	(Z)-alkenol(D23)	(E)-alkenol(D24)	secondary alcohol (B16)	leading to (D24)	overall
100	THF,65,48	25	-	5	70	-	-
100	THF,65,48	26	-	2	72	2:0	2:26
100	2,5-Me_2-THF, 91,8	86	-	-	14	-	0:86
100	2,5-Me_2-THF, 91,8	85	-	-	15	-	0:85
22	Et_2O,35,96	99	-	-	-	-	0:99
22	Et_2O,35,96	97	-	-	-	-	0:97

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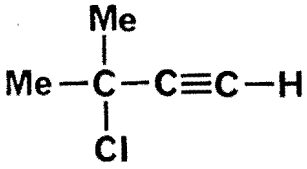

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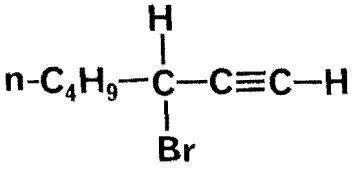

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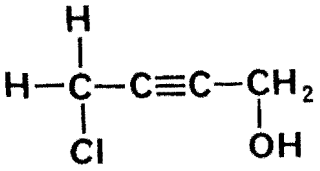

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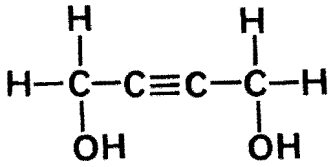

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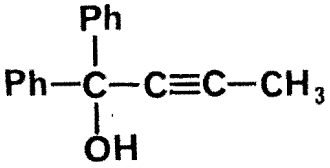

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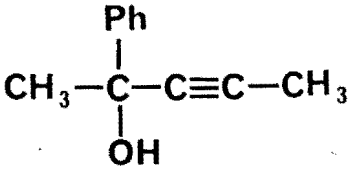

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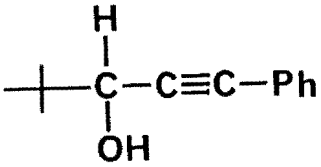

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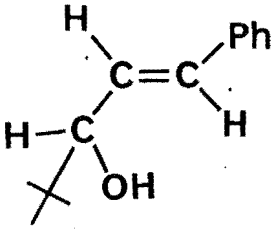

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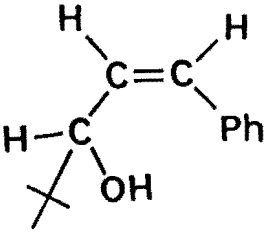

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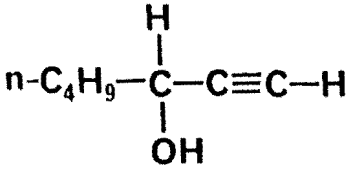

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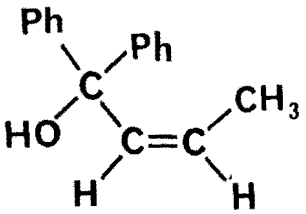

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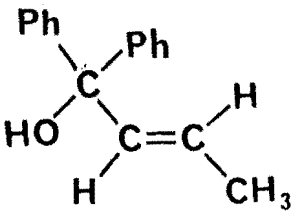

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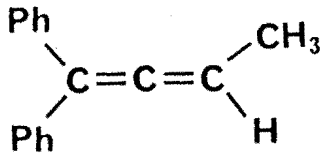

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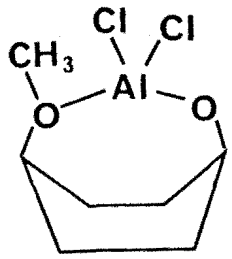

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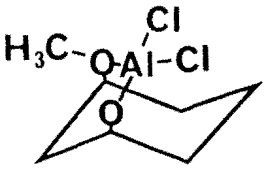

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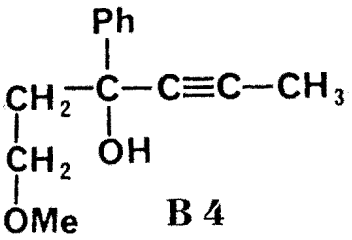

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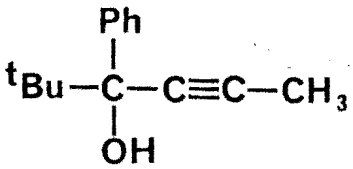

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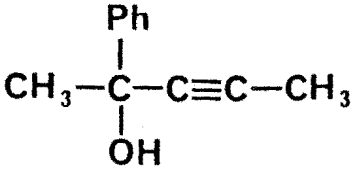

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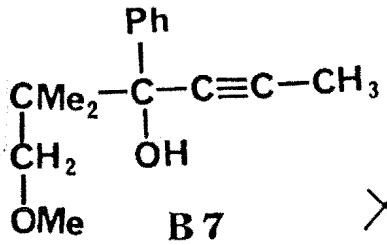

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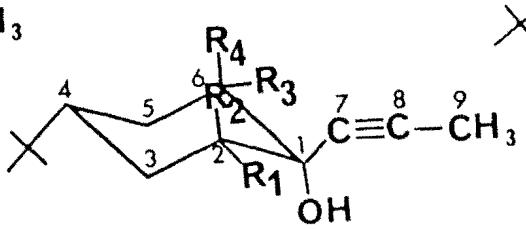
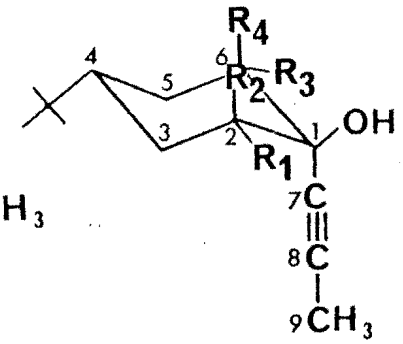
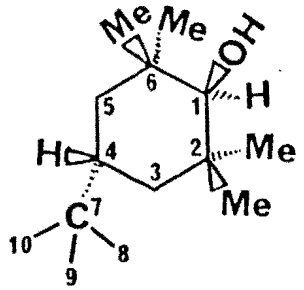


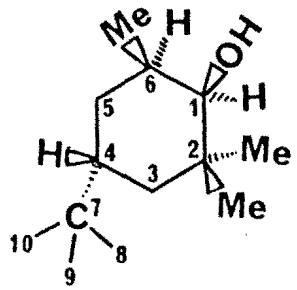




B16

B8,
B9,
B10,

B11, $R_1=R_2=R_3=R_4=H$
B12, $R_1=Me$, $R_2=R_3=R_4=H$
B13, $R_1=R_3=Me$, $R_2=R_4=H$



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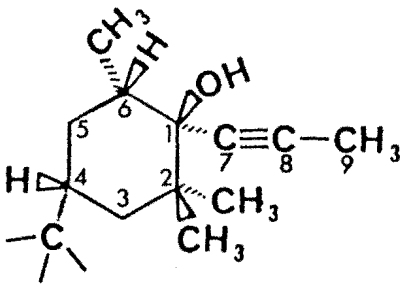

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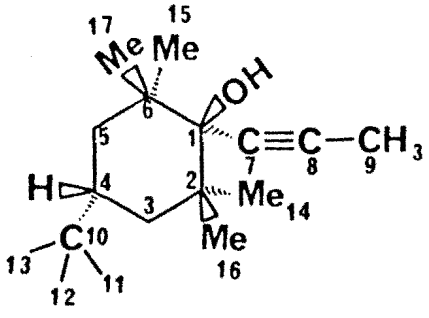

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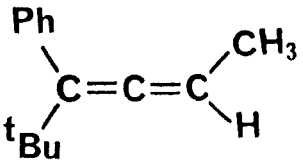

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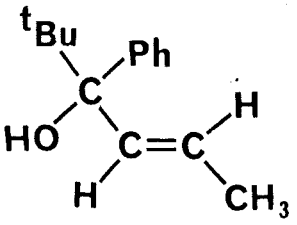

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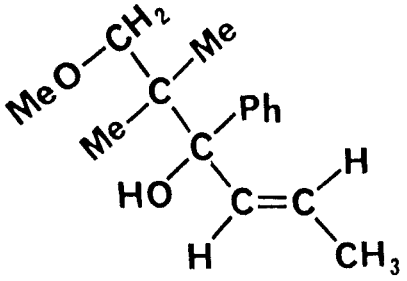

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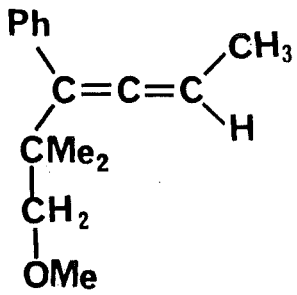

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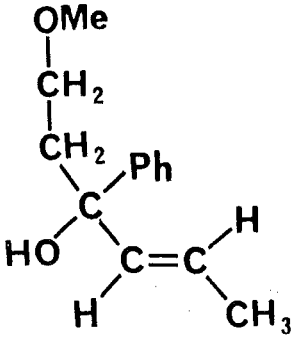

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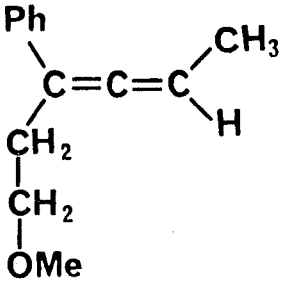

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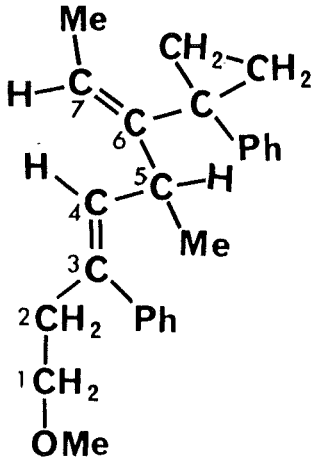

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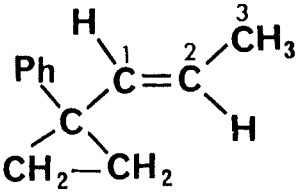

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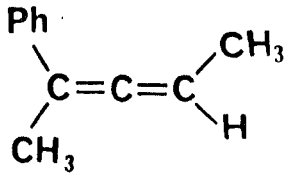

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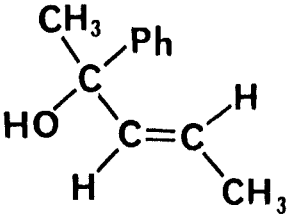

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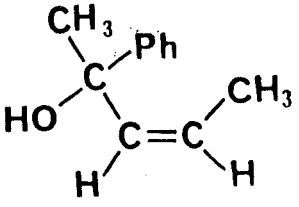

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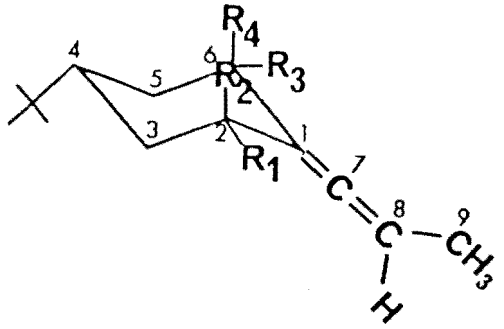

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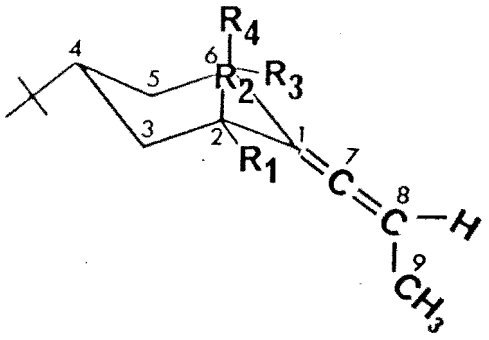

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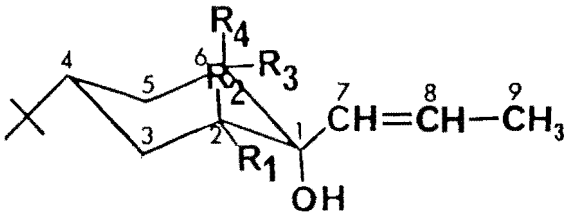
D16, $R_1=R_3=Me$, $R_2=R_4=H$

D19, $R_1=R_2=R_3=Me$, $R_4=H$

D22, $R_1=R_2=R_3=R_4=Me$



D2;(Z)-, $R_1=R_2=R_3=R_4=H$

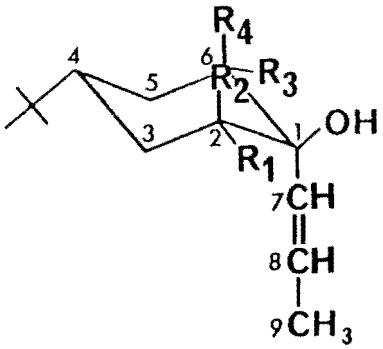
D3;(E)-, 〃

D8;(Z)-, $R_1=Me$, $R_2=R_3=R_4=H$

D9;(E)-, 〃 〃

D14;(Z)-, $R_1=R_3=Me$, $R_2=R_4=H$

D15;(E)-, 〃 〃



D5;(Z)-, $R_1=R_2=R_3=R_4=H$

D6;(E)-, 〃

D11;(Z)-, $R_1=Me$, $R_2=R_3=R_4=H$

D12;(E)-, 〃 〃

D17;(Z)-, $R_1=R_3=Me$, $R_2=R_4=H$

D18;(E)-, 〃 〃

D20;(Z)-, $R_1=R_2=R_3=Me$, $R_4=H$

D21;(E)-, 〃 〃

D23;(Z)-, $R_1=R_2=R_3=R_4=Me$

D24;(E)-, 〃

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